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1. Carbenoids
I. Title

METAL SALT CATALYZED CARBENOIDs

by

BILLY WAYNE PEACE, 1944-

A DISSERTATION

Presented to the Faculty of the Graduate School of the

UNIVERSITY OF MISSOURI - ROLLA

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ABSTRACT

The interaction of diazomalonic esters with olefins in the presence of homogeneous copper(I) and copper(II) catalyst has been examined as a function of olefin structure, solvent media, ionic strength, catalyst structure and catalyst concentration, using partial rate data.

It has been possible to determine the fine mechanistic details of the cycloproponation, C-H insertion and "dimer" forming reactions. The initial step is displacement of a ligand from copper by diazo compound in a pre-equilibrium, loss of nitrogen in the rate determining step, return of the ligand, displacement of metal from the carbenoid by olefin, followed by collapse to products.

Studies revealed the intimate involvement of catalyst with olefin as well as carbene.

A portion of the work has been published in:

1. Reprints, Division of Petroleum Chemistry, Amer. Chem. Soc., 16, (1), B81 (1971).
2. Chem. Commun., 1179, 0000 (1971).
3. Tetrahedron Lett., 3799 (1971).
4. Synthesis, 0000 (1971).
5. Synthesis, 0000 (1971).

The corpus consists of several reviews (two to be published) and nearly all experimental details and data.

THESIS PUBLICATION OPTION

Chapter I of this work has been prepared in the style utilized by Synthesis, and Chapter II in the style used by Angewandte Chemie, International Edition in English. These chapters will be submitted for publication. Chapter V has been prepared in the style utilized by the Journal of Organic Chemistry to which parts of Chapter V will be submitted for publication.

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INTRODUCTION AND STATEMENT OF PROBLEM

The past decade has seen considerable research activity concerning the generation, reactions and properties of carbenes. Most often, these studies have been concerned with the theoretical aspects of carbene chemistry, while little effort has been directed toward the use of carbene reactions in complex synthetic schemes. The use of the Simmons-Smith reaction in angular methylation (Chapter III) is a notable exception to this general trend.

The original concept of this work represents, to our knowledge, the first study directed at the development of alicyclic synthesis employing functionalized carbenes in a critical step of a reaction sequence. The final synthetic goal was the development of a stereospecific synthesis of trans fused and angularly substituted ring systems suitable for conversion to terpenes, terpenoids, and other natural products.

The general scheme involves the addition of difunctionalized carbenes (dimethoxycarbonylcarbene) to cyclohexene and substituted cyclohexenes (Figure 1). The resulting norcaranes were expected to undergo

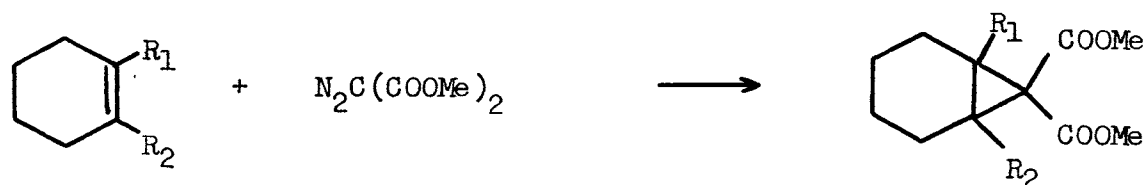
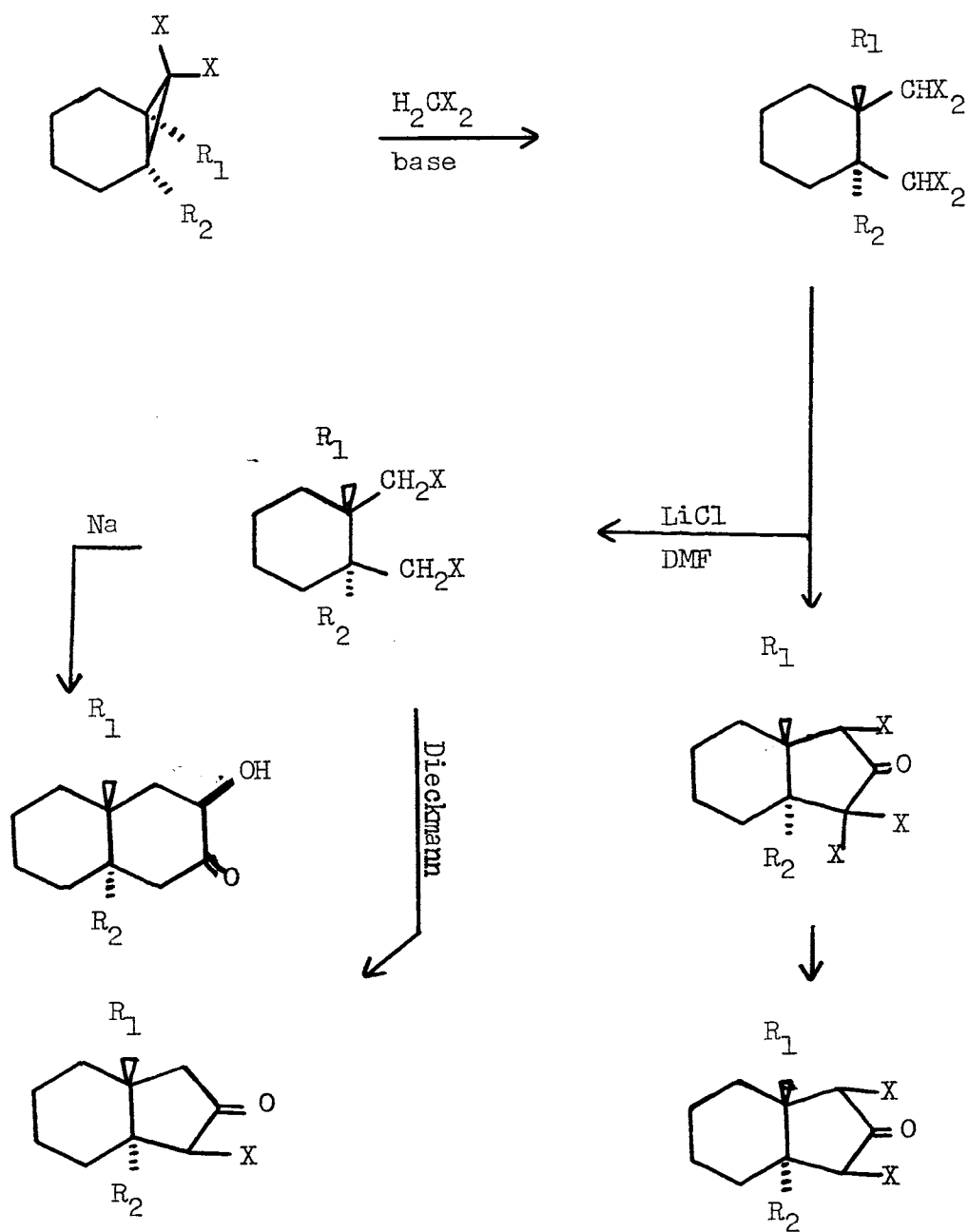


Figure 1

trans ring opening under conditions of the Michael reaction. The ring opened products, in turn, would undergo a variety of reactions leading to synthetically useful materials. (Chart 1) The utility of this

CHART I



$X=COOCH_3$, R_1 and/or $R_2=H, CH_3$

approach lies in the early introduction of the angular substituent.

The choice of dimethoxycarbonyl carbene as the carbenoid reagent was made on the basis of several considerations. First, the carbene is symmetrical and would not lead to stereoisomeric adducts. Secondly, the symmetry of the carbene would lead to adducts with simplified n. m. r. patterns. Thirdly, the methoxycarbonyl groups were expected to provide the activation of the cyclopropane ring necessary for the Michael reaction. Finally, the methoxycarbonyl groups would provide the necessary functionality for the subsequent reaction steps.

Early in this work, it became apparent that the norcaranes would be needed in large quantities and, consequently, the best possible synthesis of these materials was desirable. With this in mind, we initiated a study of the effect of various copper catalysts upon the reaction of dimethyl diazomalonate with cyclohexene and substituted cyclohexenes. At about the same time, Moser introduced trialkylphosphite copper(I) halides as catalysts for the decomposition of ethyl diazoacetate. His results led us to study the effect of these catalysts upon the reactions of diazomalonic esters.

During the early stages of the catalysts studies, it became apparent that, although copper and its salts have been used to catalyze the decomposition of diazo compounds for the greater part of a century, almost nothing is known of the mechanism by which these processes proceed. The soluble phosphite-copper complexes presented us with one of the first opportunities to study this mechanism under conditions free of surface effects and other problems normally associated with heterogeneous systems.

Thus, in the spring of 1969, we were faced with the task of

choosing between continued base catalyzed studies or a study of the catalyzed decomposition of diazomalonic esters. While the initial work on the Michael reactions had shown some interesting results, the results with respect to the original project were less than promising. On the other hand, the potential of the catalyst studies appeared to be unlimited. As stated earlier, mechanistic studies of copper catalyzed diazo decompositions are almost non-existent. In addition, the literature contains no systematic study of the behavior of diazomalonates toward cycloolefins. We also felt that, considering the present activity in the area of carbene chemistry, the catalyst studies offered the greatest potential impact upon the scientific community, and also showed greater promise of a positive thesis. These considerations led us to study the mechanism of copper catalyzed diazo decompositions as the major part of the project and to give the Michael reactions secondary considerations.

CHAPTER I

Preparation and Reactions of Diazomalonic Esters

Preparation and Reactions of Diazomalonic Esters

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Diazomalonic esters offer ready access to some classes of geminally disubstituted cyclopropanes, endo substituted bicyclo[n.1.0] systems and selectively cyclopropanated polyolefins as well as some classes of olefins bearing ether, sulfide and halogen substituents. The current scope and limitations of syntheses involving these systems are illustrated.

Introduction

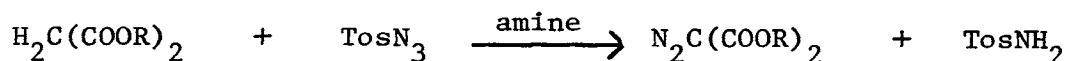
Very little information has appeared relative to the synthetic utility of diazomalonic esters. This has been a consequence of the relative difficulty and expense of their preparation and the ease of preparing diazoacetic esters which frequently offers alternate routes to similar systems. However, two useful features of diazomalonates permit syntheses which might prove difficult or impracticable with diazoacetic esters. These are the preparation of the bicyclic endo cyclopropane carboxylates and the very selective cyclopropanation of carbon-carbon double bonds of slightly differing reactivities. An additional benefit resulting from the study of diazomalonates has been the gaining of considerable insight into the features of metal and metal salt decompositions of diazo compounds and the demonstration of the synthetic advantages to be realized from the employment of soluble catalyst systems.

1. Preparation of Diazomalonic Esters

The most recent volume of Organic Reactions¹ lists hundreds of reactions involving diazoacetic esters. Far less attention has been paid to the chemistry of diazomalonates. This is mainly due to the

fact that, until recently, these diazo compounds were available only in an impure state from difficult and low yield reactions.

The first preparation of diethyl diazomalonate was carried out by diazotization of diethyl aminomalonate.² Treatment of ethyl diazoacetate with phosgene, followed by addition of ethanol,³ also gives the desired product. Both these procedures give highly contaminated material.⁴ Ciganek⁵ developed a process by which diazomalonic esters can be prepared in good yield and in high purity. This process involved formation of diethyl mesoxalate hydrazone from the corresponding mesoxalate followed by oxidation with silver oxide. The presently accepted procedure involves diazo transfer from p-toluenesulfonyl azide (tosyl azide= TosN_3) to malonic esters under the influence of a base, usually an amine (Scheme A).^{6,7} Most procedures call for the use of methylene



Scheme A

chloride or acetonitrile as solvent. Ando et al.⁸ used diethyl ether as solvent and diethylamine as base to prepare dimethyl diazomalonate in 50% yield from dimethyl malonate. A modified procedure developed in this laboratory,⁹ using benzene and triethylamine, effects this transfer in over 90% yield. Di-t-butyl diazomalonate has been prepared in exactly the same way; this reaction is much slower, giving 50% transfer after four weeks. Surprisingly, longer reaction times failed to give significantly increased yields. Unlike diazoacetates, these malonates can be obtained in almost 100% purity by careful distillation.

2. Reaction with Saturated C-H Bonds

Doering and Knox⁴ have shown that replacement of methylene hydrogens by alkoxycarbonyl groups results in carbenes of greater stability.

Unlike methylene, such stabilized carbenes have lifetimes sufficiently long, to show marked discrimination in the type of C-H bond with which they will react. The carbene series CH_2 , CHCOOCH_3 , $\text{C}(\text{COOC}_2\text{H}_5)_2$ (generated by photolysis of the corresponding diazo compounds) insert into C-H bonds with increasing selectivity. The discrimination follows the order $3^\circ > 2^\circ > 1^\circ$. The results obtained by Doering and Knox are shown in Table 1.

Table 1. Relative Reactivities of C-H Bonds toward Carbenes

Hydrocarbon	Ratio	CH_2	CHCOOMe	$\text{C}(\text{COOEt})_2$
$[(\text{CH}_3)_2\text{-CH-}]_2$	$3^\circ/1^\circ$	1.2	2.9	12.5
$(\text{CH}_3)_3\text{CH}$	$3^\circ/1^\circ$	---	3.1	21.0
$[\text{CH}_3\text{CH}_2\text{-}]_2$	$2^\circ/1^\circ$	1.0	2.3	8.4

Jones et al.¹⁰ have presented evidence showing that triplet dimethoxycarbonyl carbene is slightly more selective than the corresponding singlet carbene (Table 2). These calculations are based on

Table 2. Reactivities of Singlet and Triplet Dimethoxycarbonyl Carbene

Hydrocarbon	Ratio	Singlet	Triplet
2,3-dimethylbutane	$3^\circ/1^\circ$	13.1(12.5)*	20
n-pentane	$2^\circ/1^\circ$	3.4	5.1
n-butane	$2^\circ/1^\circ$	4.7(8.4)*	6.6

* Results from Doering and Knox.⁴

the assumption that direct photolysis of the diazomalonate ester gives rise to the singlet species, while the benzophenone-photosensitized decomposition yields the triplet. Support for this contention comes from the fact that the photosensitized reaction also gives dimethyl malonate and 1,1,2,2-tetramethoxycarbonylethane in addition to insertion products.

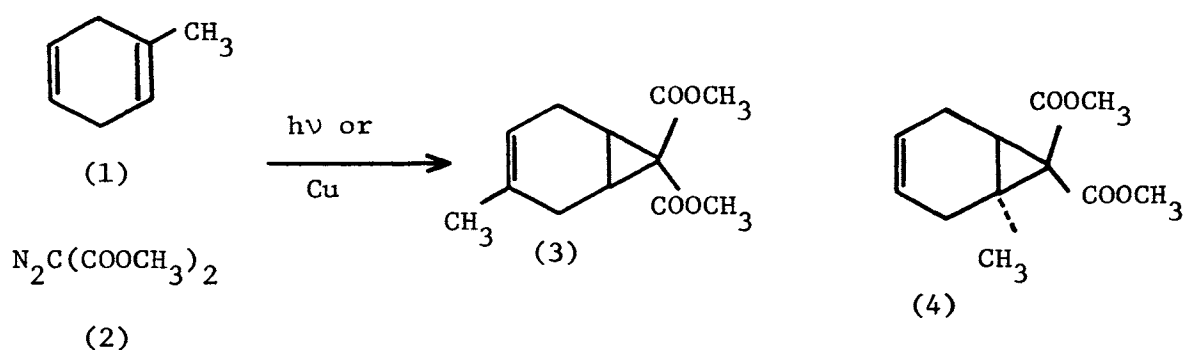
3. Reactions with Olefins

Several studies have shown that, while dialkoxycarbonyl carbene acts as an electrophile, it is much more subject to steric factors than other carbenes. In the photolysis of dimethyl diazomalonate in olefins, the cis isomer always gives higher yields of cyclopropyl adduct than the trans isomer.¹¹ Vinylic substituents increase the rate of reaction during photolysis, but there is some question as to the magnitude of the effect. Table 3 compares the results obtained by two different investigators, Karustis¹² and Neale¹³. Neale admitted he was unable to obtain reproducible results from day to day. Also, the data presented by Karustis appears to be more consistent with the data of Jones and coworkers.¹¹ Thus, Neale's results appear to be in error. Our results show that for a particular olefin the cis isomer reacts faster and cleaner than the trans isomer.

The effect of vinyl methyl groups on the course of the reaction of dimethyl diazomalonate with olefins is nicely shown in the cyclohexenyl system. In his synthesis of 7,7-disubstituted cycloheptatrienes, Berson studied the photochemical addition of dimethyl diazomalonate to cyclohexadienes.¹⁴ Irradiation of the diazo compound in 1-methyl-1,4-cyclohexadiene gave (3) as the major product and (4) as the minor product. Little or no compound (4) was formed in the copper catalyzed

Table 3. Relative Reaction Rates of Dimethoxycarbonyl Carbene with Olefins

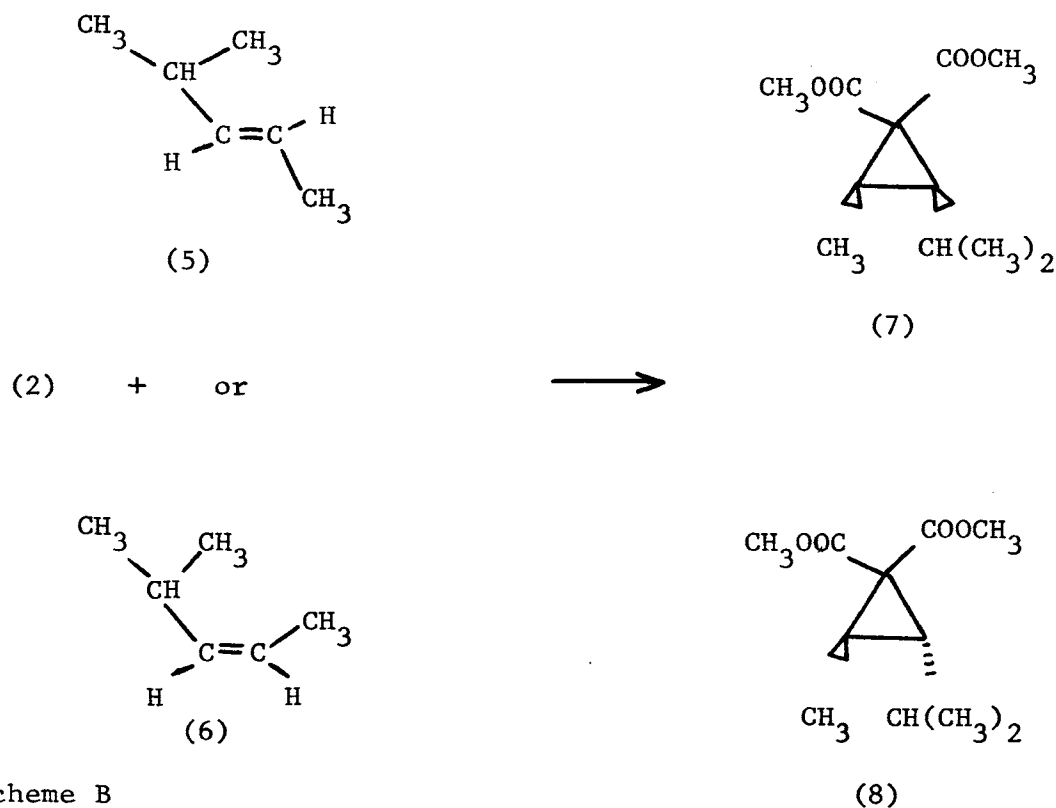
Olefin	Karustis ¹²	Neale ¹³
Isobutylene	3.75	13.7
Butadiene	3.12	10.6
<u>Cis</u> -2-butene	3.12	5.13
<u>Trans</u> -2-butene	1.84	2.93
1-butene	1.00	1.00



addition.¹⁵ Photolysis and catalyzed decomposition of dimethyl diazomalonate give far greater yield of cyclopropyl adduct with cyclohexene than with 1-methylcyclohexene. The carbene does not add to the double bond of 1,2-dimethylcyclohexene.¹⁶

The stereochemical consequences of the photolysis of diazomalonate esters in olefins have been studied by Neale¹³, Karustis¹² and Jones.^{10,11} Neale reported such reactions to be 100% stereospecific; Karustis reported irradiation in cis-2-butene to be 88% stereospecific, addition to the trans isomer being 97% stereospecific. The cyclopropyl products were accompanied by 5-6% insertion products. Jones found that

benzophenone photosensitized decompositions (conditions which favor triplet carbene) give very similar mixtures of cyclopropanes using either the cis or the trans olefin (Scheme B, Table 4).



Scheme B

Table 4. Photolysis of Dimethyl Diazomalonate in 4-methyl-2-penten^{10,11}

Conditions	(7)	(8)	Yield
<u>Cis</u> olefin	92	8	39.8
<u>Trans</u> olefin	10	90	24.3
<u>Cis</u> olefin + benzophenone	10	90	43.0
<u>Trans</u> olefin + benzophenone	14	86	----

Singlet dimethoxycarbonyl carbene appears to be less sensitive to steric factors than the corresponding triplet species. Table 5 compares the relative rates of addition of the two carbenes to various olefins. The high rates observed in the addition of the triplet carbene to butadienes is thought to be due to resonance stabilization of the di-radical.

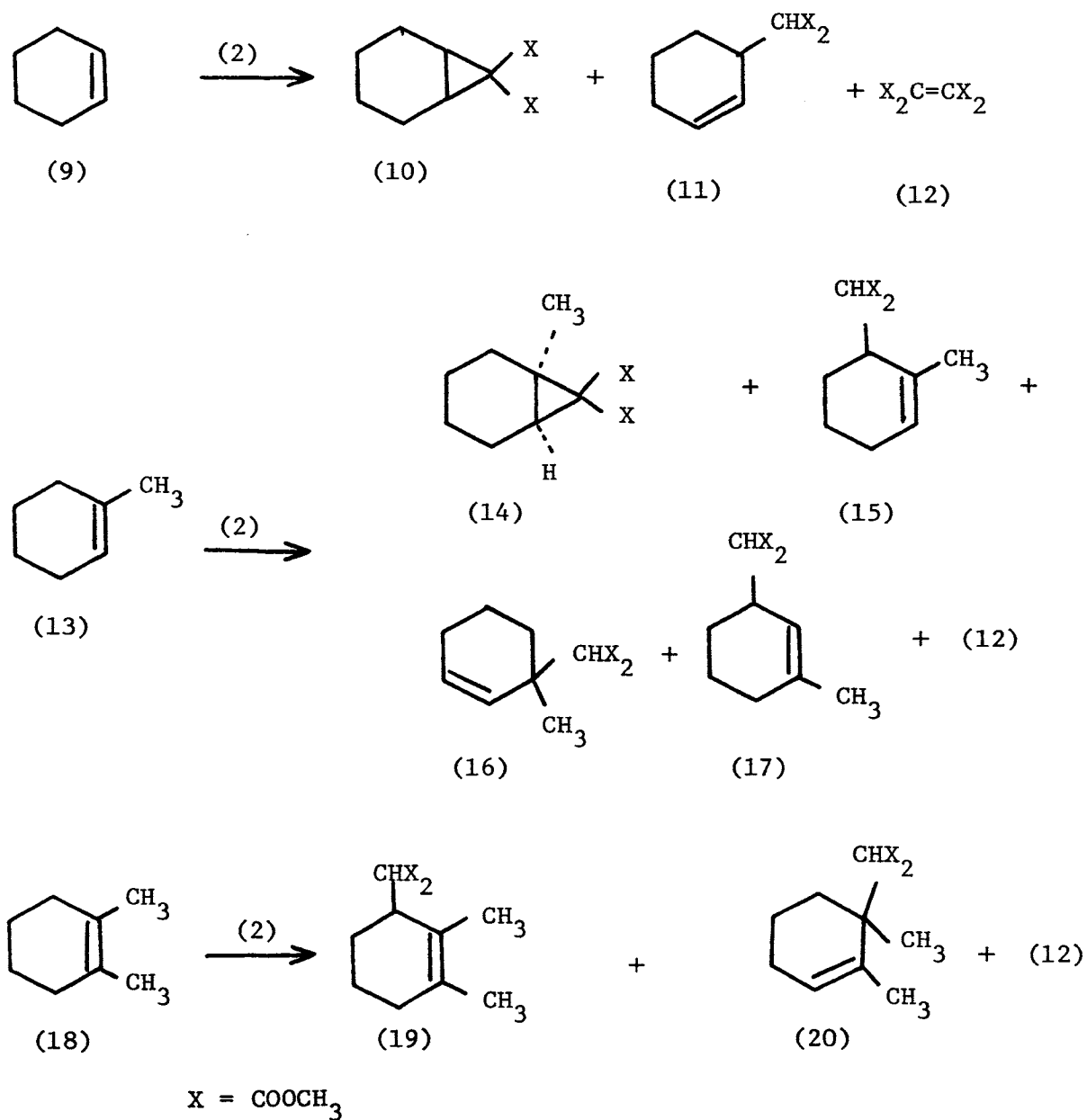
Table 5. Relative Rates of Addition of Singlet and Triplet Dimethoxycarbonyl Carbene ¹²

Olefin	Singlet	Triplet
2,3-Dimethyl-2-butene	0.88	0.33
2-Methyl-2-butene	1.00	1.00
1-Pentene	0.47	0.46
3,3-Dimethyl-1-butene	0.48	0.48
<u>Cis</u> -4-methyl-2-pentene	0.55	0.15
<u>Trans</u> -4-methyl-2-pentene	0.23	0.13
2,3-Dimethyl-1,3-butadiene	1.30	4.40
1,3-Butadiene	----	4.50

4. Copper and Copper Salt Catalysis

Relatively few copper catalyzed additions of diazomalonate esters to olefins appear in the literature. Neale¹³ was unable to isolate any products under such conditions. Carman¹⁷ treated cyclohexene with dimethyl diazomalonate in the presence of copper sulfate and isolated 7,7-dimethoxycarbonylnorcaradiene in 40% yield along with considerable amounts of tetramethoxycarbonylethylene(carbene Dimer). Carman failed to isolate any products other than the above carbene dimer and 1,1,2,2-tetramethoxycarbonylethane from attempted additions to

1-methylcyclohexene and 1,2-dimethylcyclohexene. We have found that copper catalyzed addition of dimethyl and di-*t*-butyl diazomalonates results in cyclopropyl formation with both cyclohexene and 1-methylcyclohexene. The cyclopropanes are accompanied by the formation of allylic insertion products. (Scheme C).¹⁶



Scheme C

Insertion products account for more than 50% of the products in the cases involving 1-methylcyclohexene. Under the same conditions, 1,2-dimethylcyclohexene reacts exclusively by allylic C-H insertion giving no cyclopropane. The substituted cyclohexenes yield rearranged insertion products (17,20), indicating a diradical, an ionic, and a 5-centered process as possible mechanism. It is of special note that with cyclohexene, 1-methylcyclohexene and 1,2-dimethylcyclohexene, no nonallylic or exo-cyclic insertion is observed.

We found that the choice of catalyst and reaction conditions can dramatically alter yields of the various products available (Table 6).

Table 6. Effect of Catalyst on the Reaction of Dimethyl Diazomalonate with Cyclohexene

Catalyst	(10)	(11)	(12)
Cu	38.0	1.71	8.05
CuCl	42.8	2.18	8.38
CuSO ₄	45.3	2.08	9.07
(CH ₃ O) ₃ P·CuCl	63.7	4.67	18.4
Cu(AcAc) ₂	78.1	12.4	5.92

In particular it is advisable to determine the optimum catalyst concentration and temperature when soluble catalysts are employed. Our results indicate that copper(II) acetylacetonate is the catalyst of choice (Table 7). This may not be universally true and the use of copper(I) iodide-trimethyl phosphite in hexafluorobenzene (Tables

Table 7. Product Distribution and Yields as a Function of $\text{Cu}(\text{AcAc})_2$ Concentration in the Reaction of Dimethyl Diazomalonate with Cyclohexene

Catalyst (mmole)	(10)	(12)	(11)
0.0042	6.55(1.00)	0.87(0.134)	0.87(0.134)
0.0085	6.86(1.00)	0.62(0.090)	0.86(0.125)
0.0170	51.48(1.00)	7.18(0.139)	4.63(0.090)
0.0350	40.76(1.00)	3.10(0.076)	5.58(0.137)
0.0700	71.47(1.00)	7.93(0.111)	6.19(0.087)
0.1400	78.08(1.00)	12.39(0.158)	5.92(0.076)
0.2800	69.24(1.00)	19.57(0.283)	6.44(0.093)
0.5600	55.43(1.00)	34.44(0.621)	5.00(0.090)
1.120	48.65(1.00)	20.93(0.430)	7.52(0.154)
2.240	42.04(1.00)	6.87(0.163)	4.76(0.113)
4.480	22.48(1.00)	2.82(0.125)	6.37(0.284)

Table 8. Product Distribution and Yields in the Reaction of Dimethyl Diazomalonate with 1-Methylcyclohexene using $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$ as Catalyst at 110°C

Catalyst (mmole)	(14)	(15)	(16)	(17)	(12)
0.0042	21.53(1.00)	1.51(0.070)	7.78(0.361)	19.54(0.904)	4.03(0.187)
0.0085	23.07(1.00)	1.68(0.073)	8.72(0.378)	20.12(0.874)	3.84(0.166)
0.0170	22.34(1.00)	1.63(0.073)	8.45(0.378)	19.59(0.877)	2.48(0.111)
0.0350	21.80(1.00)	1.68(0.077)	8.05(0.369)	18.91(0.868)	3.56(0.163)
0.0700	23.21(1.00)	1.80(0.077)	8.38(0.361)	20.39(0.878)	3.69(0.159)
0.1400	20.39(1.00)	1.45(0.071)	7.11(0.349)	16.90(0.830)	4.78(0.234)
0.2800	20.12(1.00)	1.54(0.077)	7.98(0.396)	19.45(0.965)	3.84(0.191)
0.5600	19.38(1.00)	1.49(0.077)	7.44(0.384)	18.71(0.966)	5.08(0.262)
1.120	18.51(1.00)	1.01(0.055)	7.63(0.358)	14.89(0.805)	7.77(0.420)
2.240	8.72(1.00)	0.40(0.046)	3.76(0.431)	9.05(1.04)	22.67(2.60)
4.480	6.77(1.00)	0.00	2.07(0.307)	4.81(0.715)	19.32(2.87)

Table 9. Product Distribution and Yields as a Function of $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$ Concentration in the Reaction Dimethyl Diazomalonate with 1-Methylcyclohexene at 85°C

Catalyst (mmole)	(14)	(15)	(16)	(17)	(12)
0.0042	8.65(1.00)	0.62(0.072)	1.46(0.169)	1.05(0.122)	2.70(0.312)
0.0085	7.24(1.00)	0.63(0.087)	0.79(0.109)	1.26(0.174)	2.32(0.320)
0.0170	4.39(1.00)	1.01(0.230)	1.47(0.334)	1.01(0.230)	4.76(1.08)
0.0350	9.99(1.00)	0.58(0.057)	2.89(0.290)	6.98(0.693)	3.20(0.320)
0.0700	6.20(1.00)	0.17(0.027)	1.11(0.179)	2.85(0.458)	1.24(0.200)
0.1400	9.59(1.00)	0.00	2.52(0.262)	9.86(1.03)	1.55(0.162)
0.2800	18.04(1.00)	1.03(0.057)	5.16(0.286)	19.72(1.09)	8.56(0.474)
0.5600	9.32(1.00)	0.49(0.052)	2.11(0.224)	9.46(1.01)	2.29(0.246)
1.120	10.66(1.00)	1.56(0.146)	2.56(0.240)	14.76(1.38)	15.24(1.43)
2.240	6.71(1.00)	0.00	2.58(0.385)	8.25(1.23)	22.17(3.30)
4.480	4.40(1.00)	0.00	1.53(0.348)	3.26(0.740)	25.52(5.80)

Table 10. Product Distribution and Yields in the Reaction of Dimethyl Diazomalonate with 1-Methylcyclohexene Using $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$ as Catalyst in Refluxing Hexafluorobenzene

Catalyst (mmole)	(14)	(15)	(16)	(17)	(12)
0.0042	12.74(1.00)	0.21(0.017)	0.94(0.074)	6.14(0.480)	6.09(0.478)
0.0085	13.08(1.00)	0.23(0.017)	0.98(0.075)	6.77(0.518)	6.40(0.489)
0.0170	11.74(1.00)	0.34(0.029)	1.01(0.086)	3.35(0.286)	3.10(0.264)
0.0350	24.62(1.00)	1.08(0.044)	1.62(0.066)	27.84(1.13)	7.99(0.324)
0.0700	11.34(1.00)	0.45(0.039)	1.56(0.137)	6.20(0.546)	3.91(0.345)
0.140	10.73(1.00)	0.91(0.084)	2.45(0.228)	5.59(0.521)	4.39(0.409)
0.280	23.34(1.00)	0.75(0.032)	1.50(0.064)	26.16(1.12)	13.87(0.594)
0.560	18.58(1.00)	0.84(0.043)	1.56(0.084)	21.53(1.16)	24.28(1.31)
1.120	13.41(1.00)	0.53(0.039)	0.83(0.061)	14.49(1.08)	39.14(2.92)
2.240	10.06(1.00)	0.56(0.055)	1.79(0.178)	12.27(1.22)	44.47(4.42)
4.480	9.19(1.00)	0.59(0.064)	2.23(0.243)	5.88(0.640)	38.65(4.21)

8, 9, 10) gives similar results. Our results with this system indicate the precautions employed by Moser¹⁸ and emphasized by Dave and Warnhoff¹ are not necessary. When optimization studies were performed using cyclohexene which had or had not been filtered through alumina to remove the last traces of peroxides, we found the absence of peroxide impurities had a deleterious effect (Table 11). We therefore developed

Table 11. Effect of Peroxide upon the Reaction of Cyclohexene with Dimethyl Diazomalonate

Catalyst	Conditions	(10)	(12)	(11)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	A	74.23 (1.00)	12.88 (0.174)	7.42 (0.101)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	B	19.38 (1.00)	2.02 (0.104)	1.79 (0.092)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	C	72.02 (1.00)	11.35 (0.157)	5.28 (0.074)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	D	67.78 (1.00)	12.09 (0.178)	6.27 (0.093)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	A	68.64 (1.00)	15.11 (0.220)	6.68 (0.097)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	B	21.96 (1.00)	1.88 (0.086)	2.08 (0.094)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	C	69.76 (1.00)	14.24 (0.204)	5.54 (0.080)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	D	67.35 (1.00)	11.77 (0.175)	5.46 (0.081)
None	C	9.44 (1.00)	1.83 (0.194)	0.00

- A. Untreated, commercial cyclohexene
 B. Commercial cyclohexene filtered through alumina
 C. Condition B, then benzoyl peroxide added
 D. Condition B, then Vazo[®] added (@DuPont's azo-bis-isobutyronitrile)

procedures to insure the presence of materials which might be derived from peroxides. These proved to be desirable for working with ultra-pure olefins.

8,8-Dimethoxycarbonylbicyclo[5.1.0] octane:

A solution of trimethylphosphite copper(I) iodide (45 mg, 0.14 mmol) and benzoyl peroxide (17 mg, 0.07 mmol) in cycloheptene (25 ml) is heated at reflux while a solution of dimethyl diazomalonate (3.16 g, 0.02 mol) in cycloheptene (25 ml) is added at the rate of 6 drops per minute. After 24 hr at reflux, the excess olefin is removed by distillation and the resulting solid recrystallized from methanol; yield: 4.29 g (80%); m. p. 61-62°.

We also surveyed the general utility of dimethyl diazomalonate as a source of bicyclo (n,1,0) systems having geminal substituents in the cyclopropane ring (Table 12).⁹ It is seen from the data in Table 12,

Table 12

that very clean reactions can be realized with cycloalkenes having no additional substituents on the olefinic carbon and with dienes other than the cyclohexadienes. Higher boiling olefins behave in a cleaner fashion than their related lower molecular weight analogs.

Our investigation with solvents (Table 13) and Ando's²⁰⁻²⁵ studies

Table 13. Solvent Effects in the Reaction of Dimethyl Diazomalonate with Cyclohexene using $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$ (0.14 mMole) as Catalyst

Solvent (90%)	(10)	(12)	(11)
Cyclohexene	63.92 (1.00)	13.25 (0.207)	4.69 (0.074)
Cyclohexane	31.23 (1.00)	52.52 (1.681)	3.90 (0.125)
Benzene	57.91 (1.00)	39.64 (0.684)	3.34 (0.058)
Hexafluorobenzene	81.00 (1.00)	15.86 (0.196)	4.24 (0.052)
Carbon tetrachloride	28.31 (1.00)	5.71 (0.202)	31.66 (1.13)
Dimethoxyethane	0.00	0.00	0.00

Table 12. Cyclopropanes from the Reaction of Dimethyl Diazomalonate with Olefins using Trimethylphosphite Copper(I) Iodide^a as Catalyst

	% Yield	m.p.	b.p./0.01 mm.
Cyclohexene	73	88.5-89	
1-Methylcyclohexene	29		53-55
3-Methylcyclohexene	76		72-75
3,5,5-Trimethylcyclohexene	80		83-85
1,3-Cyclohexadiene ^b	24	40-42	
1,4-Cyclohexadiene ^b	8	66-67	
Cycloheptene	80	61-62	
Cyclooctene	80	68-69	
1,3-Cyclooctadiene	80	59-60	

a) Commercial samples of these olefins contain sufficient peroxides that addition of benzoyl peroxide is not necessary

b) No effort was made to find the optimum catalyst concentration with the cyclohexadienes.

of allylic halides and sulfides suggest that conventional blocking groups employed to protect carbonyl and alcohol functions will not be compatible with dimethoxycarbonyl carbene or carbenoids. However, the great selectivity exhibited toward olefins of differing substitution patterns (Table 14) indicate that this feature might prove to be of synthetic utility and permit subsequent introduction of "forbidden" substituents.

Table 14. Relative Reactivities of Selected Olefins to Dimethyl Diazomalonate

	Mole ratio	(10)	(14)	<u>Cis</u>	<u>Trans</u>
Cyclohexene and 1-Methylcyclohexene	1:1	4.90	1.00		
<u>Cis-</u> and <u>Trans</u> -2-heptane	1:1			1.00	5.20

McGiboney's studies of 1,4-dihydrobenzenes,¹⁹ like those of Musso²⁶ and Berson^{14,15} indicate almost exclusive addition to the least substituted carbon-carbon double bond.

For olefins which are not liquids or are in short supply, the use of the co-solvent hexafluorobenzene is useful and tends to lead to slightly higher yields. The use of benzene as co-solvent is of lesser utility and a very real possibility exists that complex side reactions will compete in solutions of poly-substituted benzenes (vide infra). Hexafluorobenzene appears to be completely inert to the carbenoid.

The use of 7,7-dialkoxycarbonyl norcaranes and norcarene has been shown to offer a superior approach to the 7-endo-norcarane and carene carboxylate systems. A very convenient scheme to perform these inter-conversions has been developed. These procedures offer potential for the facile generation of other bicyclo[n.1.0] endo systems.²⁷

7-exo-t-Butoxycarbonyl-endo-Methoxycarbonylnorcarane:

A solution of 7,7-dimethoxycarbonylnorcarane (21.2 g, 0.10 mol) and potassium t-butoxide (11.2 g, 0.1 mol) in dry t-butyl alcohol (400 ml) is warmed to 40° under nitrogen. After 12 hr the solvent is removed using a Buchi rotovaporator with a calcium chloride drying tube in the aspirator line and replaced with fresh t-butyl alcohol. To this solution is added 15 g of 4A molecular sieves and the mixture allowed to stand, without stirring, for an additional 24 hr. The mixture is filtered, 200 ml of water added and the solution neutralized with dilute hydrochloric acid. After removal of the t-butyl alcohol, the organic layer is separated and the aqueous layer extracted three times with ether. The combined organics are washed with water, saturated sodium chloride and dried over anhydrous sodium sulfate. After removal of the ether, the oil is distilled to give the mixed ester at 76-78°/0.01 mm; yield 24.6 g (97%).

7-exo-Carboxy-7-endo-methoxycarbonylnorcarane:

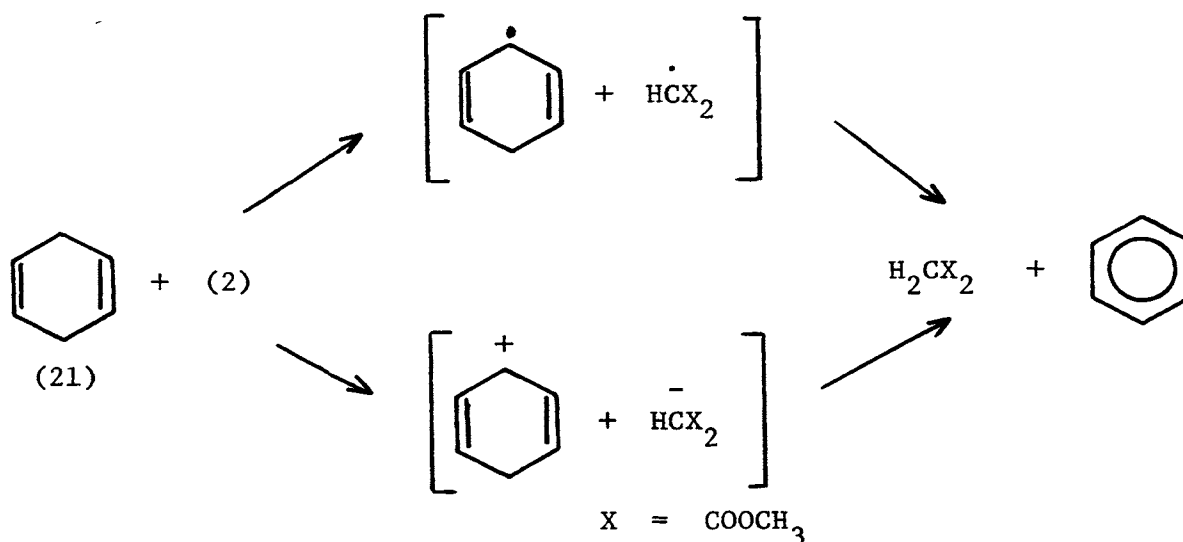
A solution of the above mixed ester (2.54 g, 0.01 mole) and anhydrous p-toluenesulfonic acid (5 mg) in dry toluene (15 ml) is heated at reflux until gas (isobutylene) evolution stops, about 3 hr. The solution is cooled and then concentrated to about 5 ml. On cooling, crystals of 7-exo-carboxy-7-endo-methoxycarbonylnorcarane are obtained; m.p. 112-114°; yield: 1.90 g (97%). The m.p. is not improved by recrystallization.

7,7-Norcaranedicarboxylate:²⁸

A solution of 7,7-dimethoxycarbonylnorcarane (5.3 g, 0.025 mol) and potassium cyanide (3.25 g, 0.05 mol) in dry dimethylformamide (75 ml) is heated at reflux for 12 hr by which time a solid forms. The solvent is removed under vacuum, the solid suspended in ether, filtered and washed several times with ether. The white solid is taken up in water (25 ml) and neutralized (hood) with dilute hydrochloric acid. The aqueous solution is extracted three times with chloroform. The combined chloroform solutions are concentrated to give 7,7-norcaranedicarboxylate, which after three recrystallizations from chloroform, melts at 186-188°; yield: 3.00 g (65%).

The addition of dimethyl diazomalonate to substituted cyclohexadienes was mentioned earlier. Mendel'shtam and coworkers²⁹ used copper stearate to catalyze the reaction of diethyl diazomalonate with 1,3-cyclohexadiene. These workers claim to have obtained a 76% yield of the norcarene. Musso and Biethan²⁶ obtained yields of 30-50% using copper and copper(I) chloride in the addition of 1,4-cyclohexadiene. Allylic insertion products were not reported for any of these reactions.

Musso and Biethan did report the isolation of up to 20% malonic ester and a comparable amount of benzene (Scheme D). This agrees well with



Scheme D

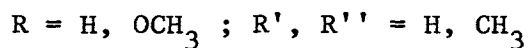
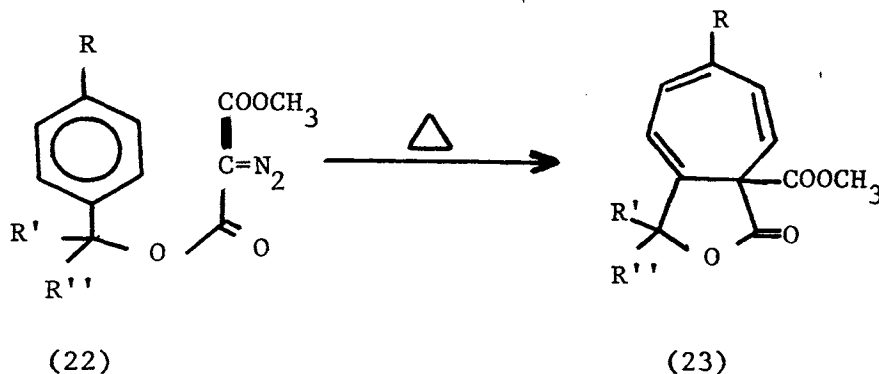
our insertion date.¹⁶ Such results are a further indication of a di-radical or ionic process. McGiboney has made similar observations in our laboratories.¹⁹

5. Reactions with Benzene

In sharp contrast to diazoacetic esters, diazomalonic esters do not normally react with aromatic compounds. Ciganek⁵ carried out thermal, photochemical and cuprous bromide catalyzed decompositions of dimethyl diazomalonate in benzene. The reactions gave complex mixtures, the major product being the carbene dimer. Karustis¹² isolated small amounts of dimethyl phenylmalonate from a similar photolysis but was unable to find any evidence of norcaradienes or tropilidienes among the reaction products.

Ledon and coworkers³⁰ have reported an intramolecular addition of a diazomalonate to an aromatic system. Thermal decomposition of the

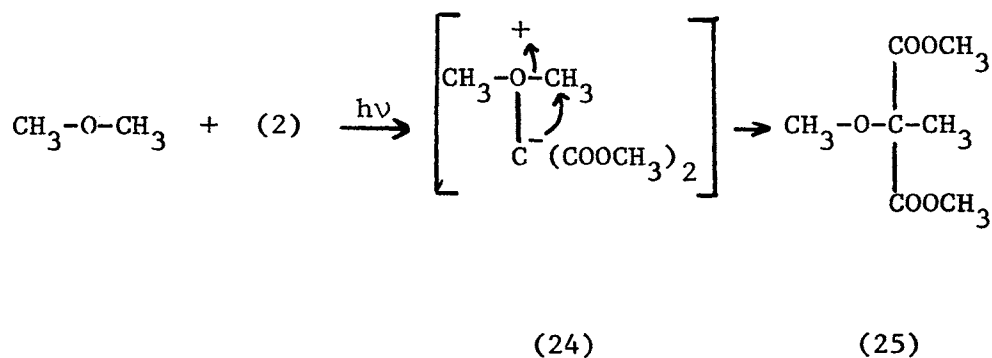
diazo compound (22) gave the tropilidene (23). In sharp contrast to



these observations, we were able to add dimethyl diazomalonate to 1,2,3,4-tetramethylbenzene using trimethylphosphite copper(I) iodide. The major product, (30%) is dimethyl 2,3,4,5-tetramethylphenylmalonate which, on the basis of bond energy considerations, can best be rationalized as resulting from rearrangement of a norcaradiene. In addition, ten other components were formed in lesser amounts and are currently being characterized.

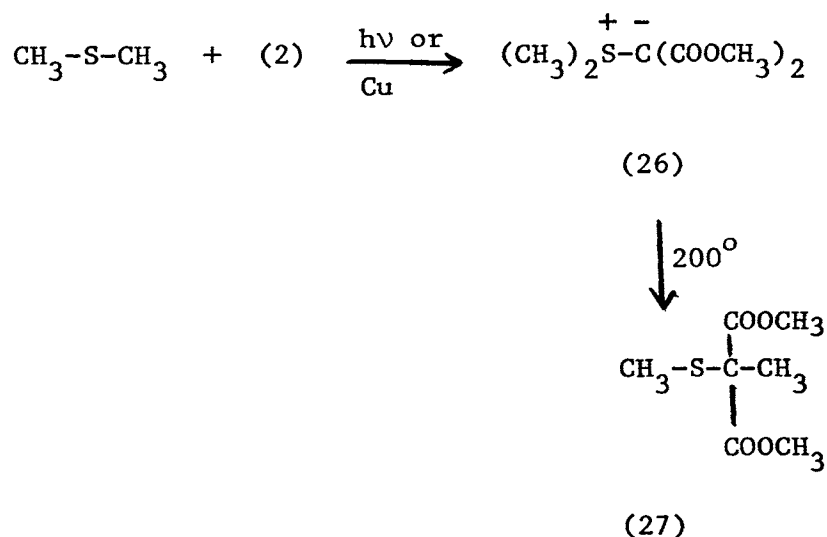
6. Reactions with Ethers and Alkyl Sulfides

Dimethyl ether reacts with dimethyl diazomalonate to give formal C-O insertion (25). It is generally accepted that direct insertion does not occur but that the reaction proceeds via the unstable oxygen ylid (24) (Scheme E).¹⁰ This contention finds support in the work of Ando's group^{20,21,22} which has shown that stable sulfonium ylids (26)



Scheme E

arise, both photochemically and catalytically, (Scheme F) through the



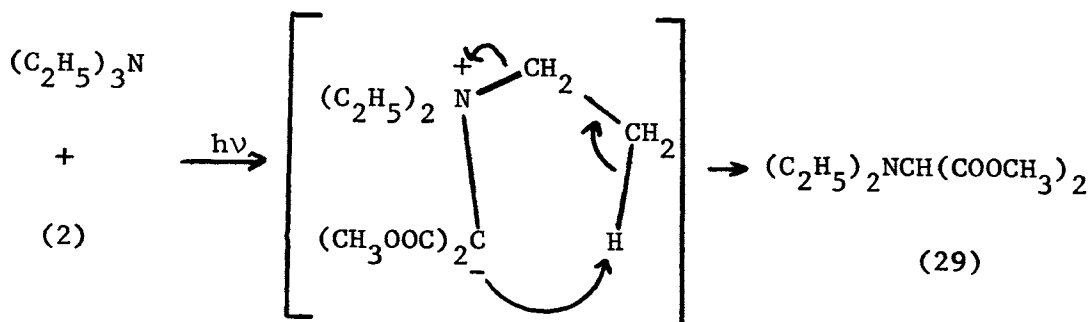
Scheme F

reaction of diazomalonate ester and aliphatic sulfides.^{21,22} The sulfonium ylids subsequently rearrange thermally to give products analogous to those obtained from reaction of the carbene with ethers (27).^{21,22} Competition studies showed the carbene to react with sulfides four times faster than with cyclohexene. Benzophenone sensitized photodecomposition of the diazo compound failed to generate the ylid, thus indicating

that only singlet carbene is capable of undergoing the ylid forming reaction.

7. Reactions with Amines

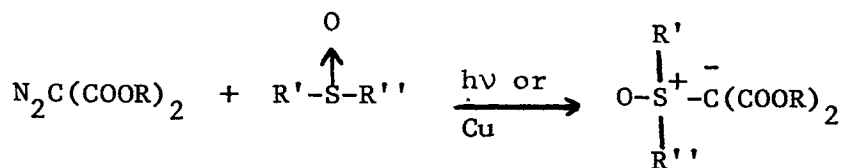
Dimethoxycarbonyl carbene reacts with amines to give insertion products (29).²¹ The reaction is thought to proceed through a nitrogen ylid (28) (Scheme G) similar to the oxygen and sulfur ylids.



Scheme G

8. Reactions with Sulfoxides

Stable sulfoxonium ylids (30) result from the reaction of dimethylsulfoxide with a variety of diazo compounds, including dimethyl and diethyl diazomalonate.³¹ Ando and coworkers²⁰ obtained similar results under photolytic and copper catalyzed thermal conditions with several alkyl and aryl sulfoxides.



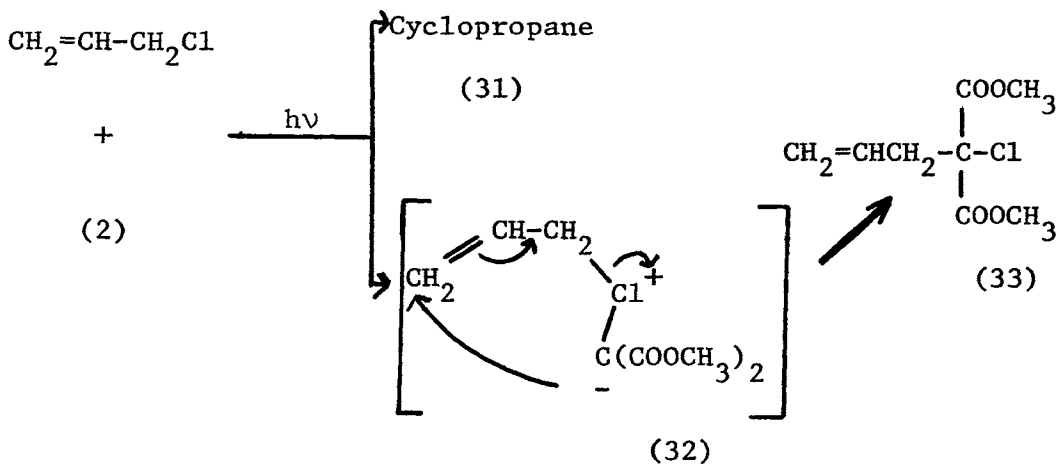
(30)

9. Reaction with Thioketones

Kaufman and Weininger³² reported that irradiation of equimolar amounts of diethyl diazomalonate and thiobenzophenone gave γ -butyrolactone as the major product. Although the exact mechanism is not known, the possible intermediacy of a sulfur ylid was suggested.

10. Reactions with Allyl Sulfides and Halides

Ando and coworkers^{8,23-25} have made an extensive investigation into the reaction of dimethyl diazomalonate with allyl halides and sulfides. These reactions give cyclopropyl products along with C-Cl and C-S insertion products. The insertion is not direct, but proceeds through a halonium or sulfonium ylid (Scheme H). The authors presented compelling evidence based on



Scheme H

dilution data (Table 15) that, like addition to alkyl sulfides and ethers, only the singlet carbene can undergo the insertion reaction.

Table 15. The Effects of Solvents on the Photochemical Decomposition of Dimethyl Diazomalonate in Allyl Chloride

Solvent	Concentration ^{a)} %	33/31	Overall yield %
None	0	2.35	76
None + Ph ₂ C=O	0	0.056	93
C ₆ H ₁₂	10	3.39	64
C ₆ H ₁₂	50	2.52	26
C ₆ H ₁₂	90	1.95	5
CH ₂ Cl ₂	10	2.38	60
CH ₂ Cl ₂	50	2.20	35
CH ₂ Cl ₂	90	1.17	10
CH ₂ Br ₂	10	2.19	36
CH ₂ Br ₂	50	1.60	14
CH ₂ Br ₂	90	0.06	4
CH ₂ I ₂	10	1.94	27

a) Mole per cent of solvents

Our own investigations were supported with university monies and in part by NSF Grants GP-3768 and GY-3514.

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CHAPTER II

Decomposition of Diazo Compounds by Soluble Metal Complexes

Decomposition of Diazo Compounds by Soluble Metal Complexes

B. W. Peace and D. S. Wulfman^[*]

Abstract: Evidence is presented demonstrating the usefulness of soluble metal complexes for promoting the generation of carbenoids from diazo compounds and the factors influencing and influenced by diazoalkane-metal complex systems.

1. Introduction

Since the original discovery that metals and their salts catalyze the decomposition of diazo compounds, procedures have been extensively developed to utilize this phenomenon. Primary emphasis has been on the employment of copper(0), and copper(I) and copper(II) salts. Some of these have been soluble or partially soluble in the reaction mixtures, but primary usage has been with heterogeneous systems. As we shall demonstrate, the use of homogeneous systems offer considerable advantage and permits more precise examination of the mechanistic aspects of the reactions of diazo compounds and catalysts.

The study of diazo compounds and their decompositions dates from the preparation of diazomethane by von Pechmann^[2] in 1894 from N-nitrosomethylurethane and alkali. Their general preparation and chemistry have been the subject of a number of monographs, chapters, and reviews, the most recent being those of Kirmse^[3], Smith^[4], Millar and Spengall^[5], and Cowell and Ledwith.^[6] In addition, more specialized reviews dealing with the chemistry of diazo compounds, carbenes or carbenoids have appeared. These include reviews on diazomethane chemistry by Gutsche^[7] and Hopps^[8] and several reviews on halomethylmetal compounds.^[9,10,11] Fischer^[12] recently reviewed the chemistry of stable transition metal carbonyl carbene complexes. The stereochemistry of carbene additions was covered by Closs.^[13] Of particular importance to our recent studies

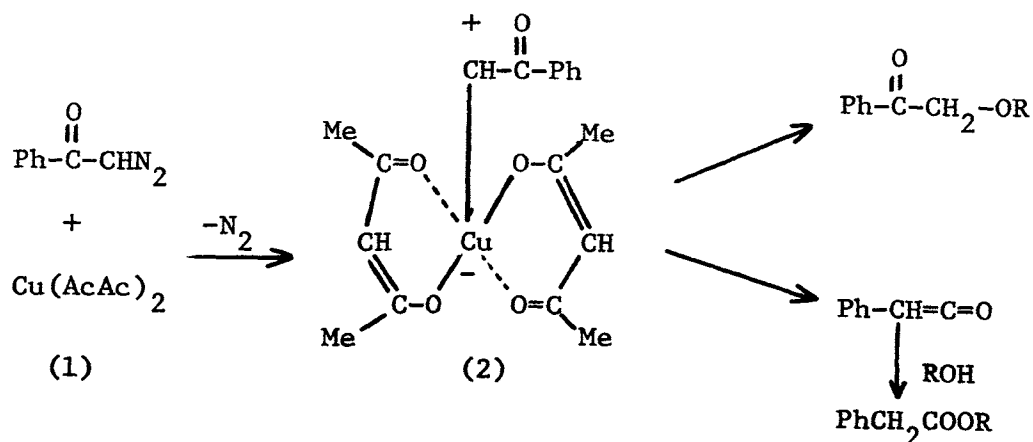
is the review by Dave and Warnhoff^[14] on the chemistry of diazoacetic ester.

The decomposition of diazocompounds by boron trifluoride^[15], trialkylborates,^[16,17] metals and metal salts^[18,19,20] will not be dealt with here. This survey is primarily concerned with homogeneous and/or metal complex catalyzed decompositions of diazo compounds. Special emphasis will be placed on the reactions of the resulting species with olefinic substrates.

2. Copper Complexes

Takebayashi and coworkers^[21] have studied several reactions of diazo compounds catalyzed by bis(acetylacetonate)copper(II). In the presence of $\text{Cu}(\text{AcAc})_2$, α -diazoacetophenone and alcohols react to give alkoxyacetophenone; the addition of tertiary amines to the reaction mixtures suppresses ether formation in favor of the expected phenylacetic ester.^[21]

These results were explained in terms of a carbene-metal chelate complex (2). The acetylacetonates of nickel and lead were active catalysts but not as effective as the copper complex. The corresponding complexes of aluminum, barium, beryllium, calcium, cadmium, cobalt, iron, magnesium, manganese, and zinc manifested no activity.



In a later paper,^[22] the same group described the $\text{Cu}(\text{AcAc})_2$ catalyzed addition of α -diazacetophenone to a variety of olefins, the yields of cyclopropyl adducts were moderate to poor (Table 1). The selectivity of the carbene-metal chelate complex is shown by its

Table 1. $\text{Cu}(\text{AcAc})_2$ Catalyzed Addition of α -Diazoacetophenone of Olefin

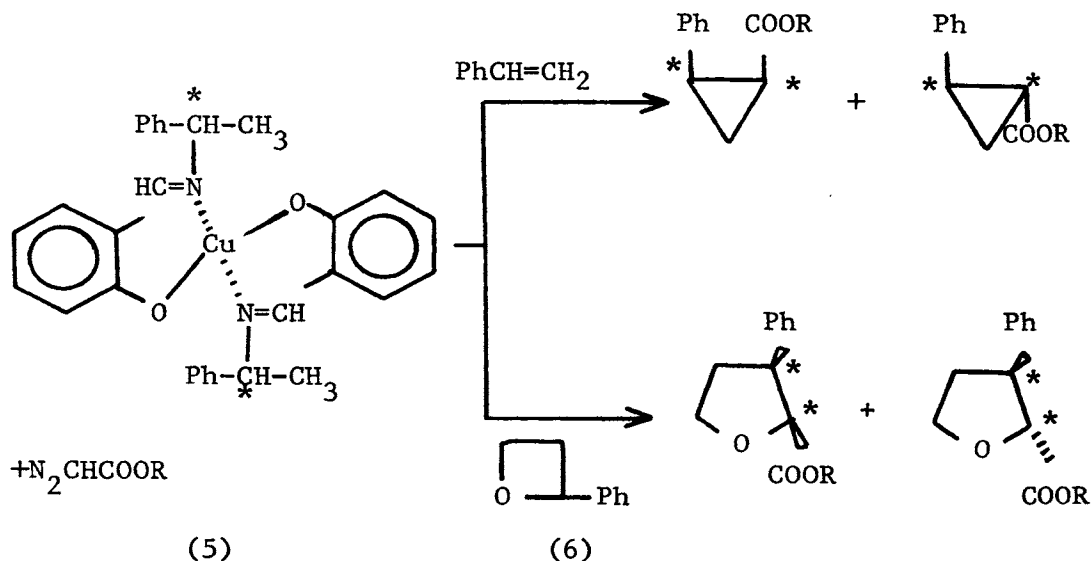
Olefin	Yield %
Vinyl acetate	58
Cyclohexene	51
<u>Cis</u> -stilbene	19
<u>Trans</u> -stilbene	5

Surprisingly, $\text{Cu}(\text{AcAc})_2$ failed to catalyze the addition of diphenylcarbene to either cyclohexene or ethyl vinyl ether. However, an enamine of cyclohexanone added the carbene to give 62% yield of cyclopropyl adduct. The demand of the carbenoid for electron rich double bonds (Cyclohexene compared to the enamine) appears to support a carbene-copper chelate complex postulated by Takebayashi.^[22] It may be significant that recovery of as much as 90% of the copper chelate was reported. This has been assumed to demonstrate that $\text{Cu}(\text{AcAc})_2$ is serving as a true catalyst.

When the methyl groups of $\text{Cu}(\text{AcAc})_2$ are replaced by phenyl, ethoxy or trifluoromethyl, varying ratios of azine (4) to ethylene products (3) were obtained from the decomposition of diphenyldiazomethane.^[24] However, no definite trend was established.

In contrast to the failure of $\text{Cu}(\text{AcAc})_2$ to catalyze the addition of diphenyldiazomethane to cyclohexene, we have shown the complex to be an excellent catalyst for the addition of dimethyl diazomalonate to cyclohexene.^[25] The yield of 7,7-dimethoxycarbonylnorcarane was found to be highly dependent upon catalyst concentration. At optimum concentration, the copper chelate gave twice the yield as that obtained using heterogeneous copper salts. In addition, at high concentrations of $\text{Cu}(\text{AcAc})_2$ it appears that a small amount of metallic copper is liberated during the reaction. This in turn suggests the possibility that all three valence states are present and casts doubt as to the nature of the actual catalyst species. Fortunately, experiments have been performed which strongly indicate that copper(II) is the most active catalyst species (*vide infra*).

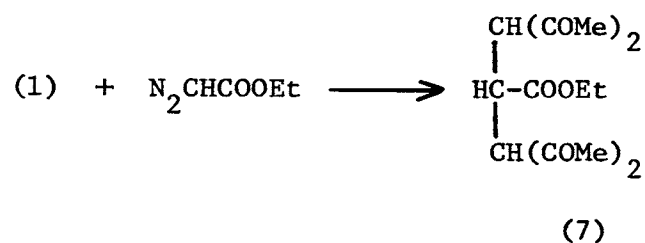
The intermediacy of copper carbenoids in the decomposition of diazo compounds as catalyzed by copper chelates was shown by Nozaki et al.^[24,26] The chiral copper chelate, bis-N-(R)- α -phenethylsalicylaldiminato copper(II), (5) was prepared and found to decompose diazo compounds readily. Ethyl diazoacetate, in the presence of this chelate, reacted with both styrene and 2-phenyloxetane (6) to give asymmetric products.



Similar results were obtained in the reaction between diazomethane and cis, trans, trans-1,5,9-cyclododecatriene and trans-propenylbenzene. The optical yields were 6-8% in all cases. Nozaki considered such yields to be low; but, considering the proximity of copper and the asymmetric centers, we feel the optical yields are quite good. The intermediacy of a free carbene as a possible explanation for the low optical yield was discounted on the basis of dilution data. Even a partial asymmetric synthesis of this type does indicate strong coordination between copper and carbene.

The addition of diazoacetaldehyde to tetramethylethylene proceeds to give the cyclopropyl adduct in 25% yield in the presence of $\text{Cu}(\text{AcAc})_2$.^[27]

The reaction of ethyl diazoacetate with $\text{Cu}(\text{AcAc})_2$ itself has been studied by Sato.^[28] The main product (7) was found to result from a reaction between one carbene species and two molecules of acetylacetonate. Oxidation of the chelate by cupric ion accounts for the product.

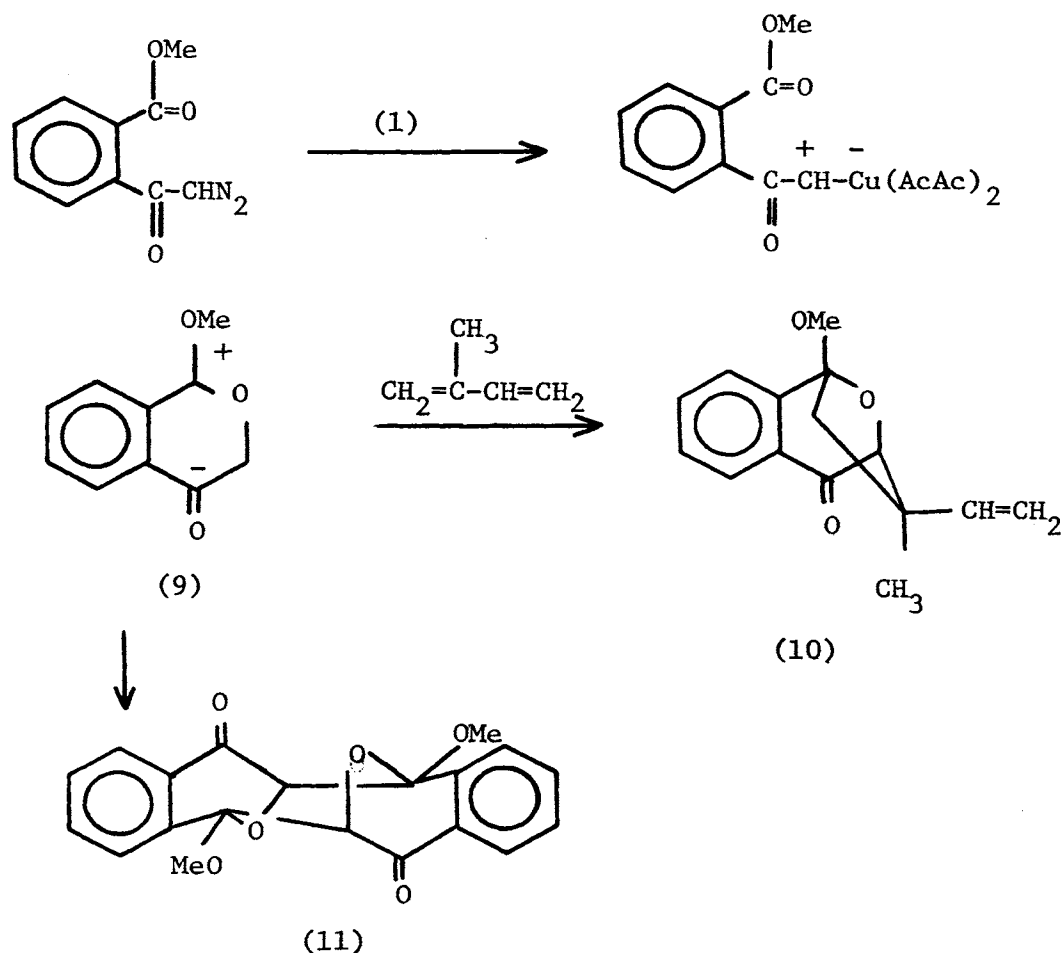


Diethyl maleate, a frequent product from diazoacetic ester reactions, was isolated in 45% yield. It is mechanistically significant that the thermodynamically more stable diethyl fumarate was not reported to be among the products.

One of the few studies which has compared the catalytic activities of copper chelates to copper salts was carried out by Hammond and co-workers.^[29] The copper(II) dipivaloylmethide complex was shown to be inferior to copper salts in the addition of α -diazoacetophenone to cyclohexene. However, all the reactions were carried out at 28°C; and no effort was made to optimize reaction conditions or catalyst concentrations. It is dangerous to draw conclusions from any study which fails to examine the obvious variables of temperature, concentration, and olefin structure (vide infra).

The $\text{Cu}(\text{AcAc})_2$ catalyzed reaction of α -diazoacetophenone with aromatic aldehydes and ketones has been extensively investigated. Benzaldehyde and acetophenone yield the corresponding tetrahydrofurans and dioxolanes.^[30] The reactions can be explained in terms of a betaine intermediate resulting from the interaction of the carbene-copper chelate

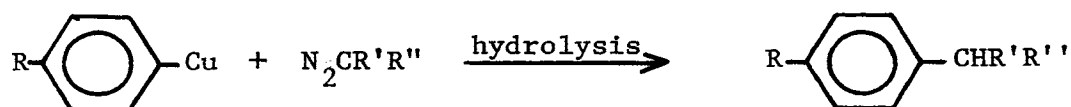
complex with the ketone or aldehyde carbonyl group. A similar intramolecular process occurred during the decomposition of o-methoxycarbonyl- α -diazoacetophenone (8).^[31] In this case, the intermediate betaine (9) was trapped with conjugated dienes to furnish (10) and (9) dimerized to furnish (11).



It is of interest, but not of great synthetic utility, that aryl copper compounds are capable of decomposing diazo compounds. Cairncross and Sheppard^[32] found that typical carbene products resulted when ethyl diazoacetate or bis(trifluoromethyl)diazomethane were treated with pentafluorophenylcopper. In the reactions of ethyl diazoacetate in

inert solvents, maleate and fumarate esters were generated in a 1:1 ratio. This might be taken to indicate the formation of free carbene; but, the authors discounted the intermediacy of free carbene in favor of the ylid, $C_6F_5Cu^-C^+RR'$, while presenting no supporting data.

Sato and Watanabe^[33] devised a modification of this reaction which is useful for preparing substituted aralkyls (Scheme 1, Table 2).



Scheme 1

Table 1. Products and Yields from the Reaction of Aryl Copper with Diazo Compounds.

Diazo-compound	Copper Compound	Product	Yield
$\text{N}_2\text{CHCO}_2\text{Et}$	PhCu	$\text{PhCH}_2\text{CO}_2\text{Et}$	51.5
N_2CHCOPh	PhCu	PhCH_2COPh	34.8
N_2Ph_2	PhCu	Ph_3CH	41.0
		Ph_3COH	38.5
$\text{N}_2\text{CHCO}_2\text{Et}$	p-MeC ₆ H ₄ Cu	p-MeC ₆ H ₄ CH ₂ CO ₂ Et	45.5
N_2CHCOPh	p-MeC ₆ H ₄ Cu	p-MeC ₆ H ₄ CH ₂ COPh	31.0

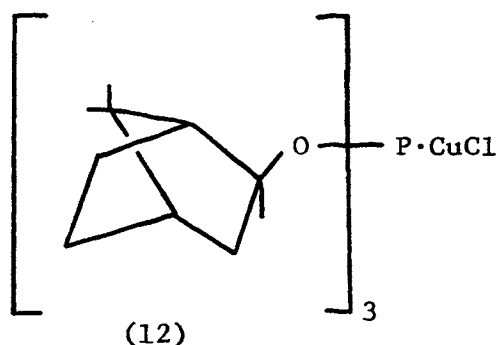
In the reactions involving ethyl diazoacetate, 40% ethyl maleate was obtained as a by product. This is in sharp contrast to the fluorinated arylcoppers^[32] which gave a 1:1 ratio of the carbene dimers.

The most comprehensive study of the mechanism of copper catalyzed decomposition of diazo compounds previously reported was carried out by Moser.^[34,35] In his studies ethyl diazoacetate was added to olefins

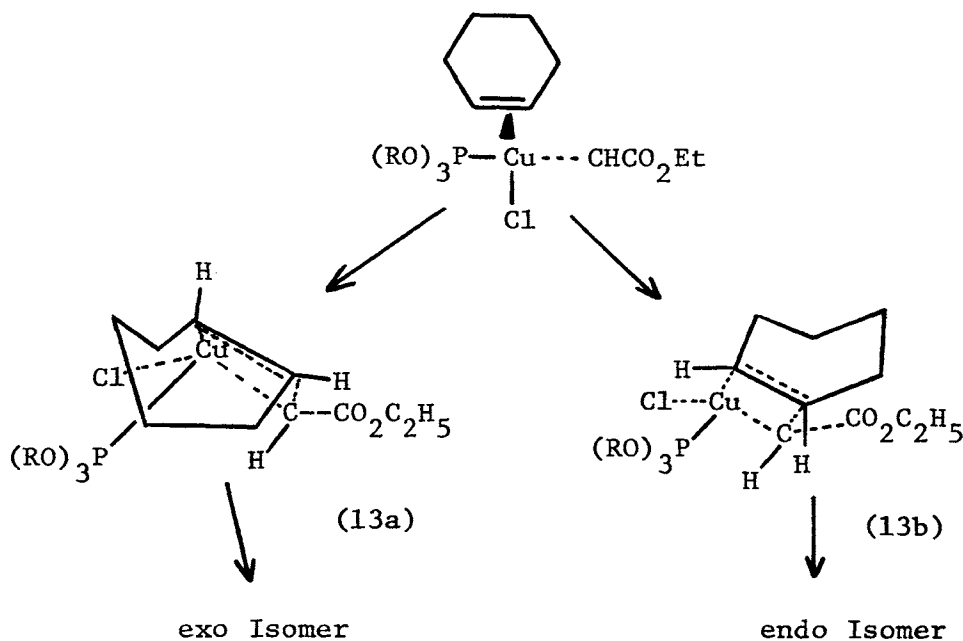
using soluble copper(I) phosphite complexes of the type $(RO)_3P \cdot CuX$, where R was alkyl or aryl and X was Cl, Br, I or CN. These catalysts decompose diazoacetic ester readily at room temperature. Using cyclohexene as substrate and tris(n-alkyl)phosphite copper(I) halides, the exo-endo ratio of the norcarane esters decreased as the number of carbon atoms in the phosphite increased. The effect was not linear and no change was observed above five atoms. This effect was shown to be due to steric factors by systematically increasing the degree of branching of the phosphite.

Catalysts of the type $(Cl-(CH_2)_n-O)_3P \cdot CuCl$ were found to give an increase in the exo-endo ratio as n increased. In cases where substituted aryl phosphites were part of the catalyst, the exo-endo ratio gave a good fit to the normal Hammett parameters.

The optically active tribornylphosphite copper(I) chloride (12)



gave a slightly optically active cyclopropane from the reaction of ethyl diazoacetate and styrene. The optical yields were low (3%), compared to Nazaki's work (6-8%), but, the copper atom in the phosphite complex is further away from the optical center. Moser claims his results require a transition state in which all reacting species (Catalyst, carbene, and olefin) are present (Scheme 2).



Scheme 2

There does seem to be some question as to the actual catalytic species present when the phosphite catalysts are used. Moser noted that the catalyst solution turned brown early in the addition of the diazo compound. House and Blankley^[36] noted the appearance of an apparently insoluble material in all room temperature reactions utilizing the trialkylphosphite-copper(I) halide catalyst.

We have extended the use of trialkylphosphite copper(I) halide catalyst to the decomposition of dimethyl diazomalonate and di-*t*-butyl diazomalonate. At room temperature the catalysts decompose diazomalonate ester very slowly and the main products are the esters of the ethylene tetracarboxylate. Addition of dimethyl diazomalonate to a variety of olefins has been accomplished at reflux temperatures.^[37,38] Higher yields of cyclopropyl products are obtained as the boiling points of the olefins increase.

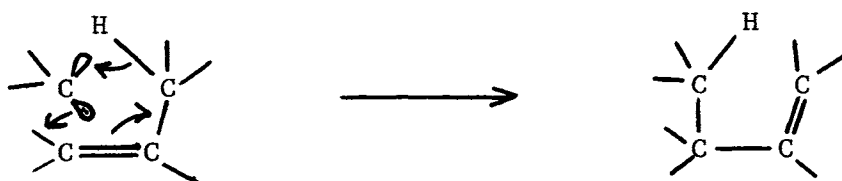
A particularly interesting and, perhaps to some, disturbing set of conclusions are required to account for the structures of the allylic

insertion products^[38,39] in the reaction of dimethyl diazomalonate with substituted cyclohexenes (compounds 14, 19, 24) because cis-2-heptene undergoes completely stereospecific cyclopropanation under identical conditions (Table 3).

Table 3. Products and Yields from the Reaction of Dimethyl Diazomalonate with 2-Heptenes.

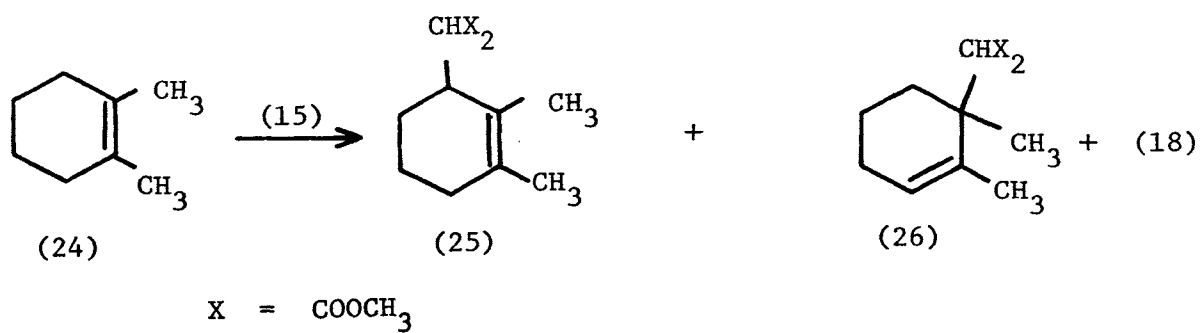
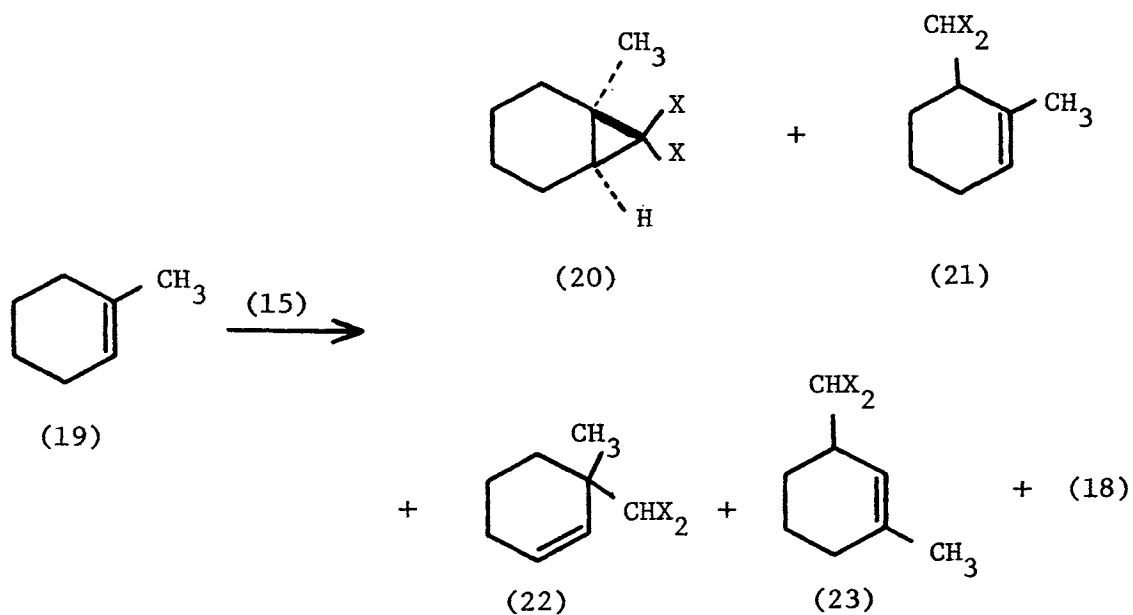
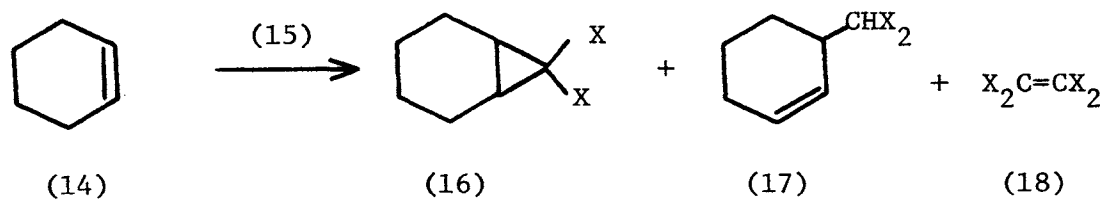
0.14 mmole of (CH ₃ O) ₃ P·CuX	2-Heptene	Temp. °C	Cyclopropane		Insertion	Dimer
			Cis	Trans		
X = I	<u>Cis</u> (96%)	98	95.6	Trace	0.52	3.36
I	<u>Cis</u> (96%)	85	92.1	Trace	3.30	4.64
Br	<u>Cis</u> (96%)	85	87.6	Trace	7.08	5.32
Cl	<u>Cis</u> (96%)	85	81.3	Trace	12.8	6.00
I	<u>Trans</u> (99%)	98	0.00	76.0	6.60	17.4
I	<u>Trans</u> (99%)	85	0.00	69.8	18.6	11.6
Br	<u>Trans</u> (99%)	85	0.00	72.5	18.4	9.20
Cl	<u>Trans</u> (99%)	85	0.00	41.7	35.2	23.1

The presence of rearranged products can in part be treated as resulting from the 5-centered process shown in Scheme 3. However, this scheme



Scheme 3

cannot account for the formation of (23). We therefore must conclude that at least a portion of the rearranged products arise from a two-step



process. Thus we see a stereospecific cyclopropanation occurring under conditions conducive to triplet like processes. Musso^[41] has reported the isolation of up to 20% diethyl malonate and a comparable amount of benzene from the reaction of diethyl diazomalonate with 1,4-cyclohexadiene.

The inescapable conclusion is that stereospecificity need not be and indeed is not necessarily indicative of singlet like behavior. Closs,^[13] amongst others, has cautioned against such an assumption for carbenes in general. The correlation of spectroscopic spin states, like orbital symmetry, with the chemical behavior of molecules, can be especially misleading in the presence of transition metals.^[43] It is very likely that in the catalyst-carbene-olefin complex involved in cyclopropanation, free rotation about the single bond formed in any multistep cyclopropanation reaction is possible.

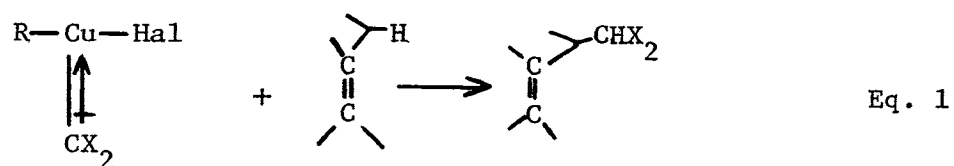
A comparison of the various catalysts generally employed for "carbene" generation was made with cyclohexene (Table 4) and 1-methylcyclohexene (Table 5).^[37,39] In order to perform these studies it was

Tables 4 and 5

necessary to examine the variable, concentration, when operating in the homogeneous systems. The fact that there should be optimum catalyst concentrations for the various products (Tables 6 and 7) is not in

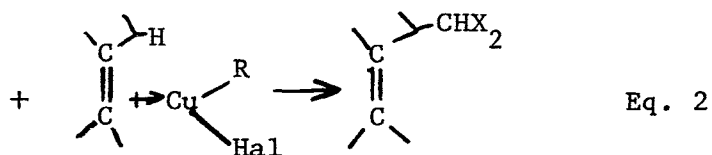
Tables 6 and 7

itself surprising. However, the net effect of these partial rate studies is the ability to assign apparent molecularities to the formation of dimer, allylic C-H insertion products and cyclopropanes (Equations 1-5).^[44,45]

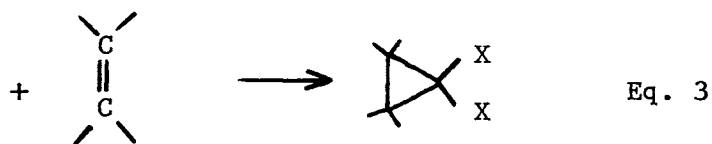


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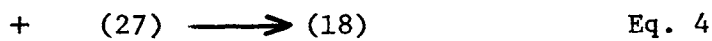
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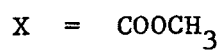


Table 4. Effect of Method of Carbene Generation on Yield and Product Distribution in the Reaction of Dimethyl Diazomalonate with Cyclohexene.

Catalyst	(16)	(17)	(18)
Cu	38.0 (1.00)	1.71 (0.045)	8.05 (0.105)
CuCl	42.8 (1.00)	2.18 (0.051)	8.38 (0.097)
CuSO ₄	45.3 (1.00)	2.08 (0.046)	9.07 (0.099)
(CH ₃ O) ₃ P·CuCl	63.7 (1.00)	4.67 (0.074)	18.4 (0.144)
(CH ₃ O) ₃ P·CuI	73.53 (1.00)	5.98 (0.081)	11.5 (0.157)
Cu(AcAc) ₂	78.1 (1.00)	5.92 (0.076)	12.4 (0.158)

Table 5. Effect of Method of Carbene Generation on Yield and Product Distribution in the Reaction of Dimethyl Diazomalonate with 1-Methylcyclohexene

Catalyst	(20)	(21)	(22)	(23)	(18)
Cu	22.9 (1.00)	1.23 (0.054)	4.13 (0.180)	18.5 (0.810)	5.64 (0.122)
CuCl	19.1 (1.00)	1.45 (0.076)	3.76 (0.197)	17.5 (0.915)	4.83 (0.125)
CuSO ₄	24.8 (1.00)	2.49 (0.100)	6.07 (0.244)	24.0 (0.0965)	7.36 (0.146)
(CH ₃ O) ₃ P·CuCl	29.6 (1.00)	2.30 (0.077)	10.7 (0.360)	26.0 (0.878)	5.15 (0.086)

Table 6. Product Distribution as a Function of $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$ concentration in the Reaction of Dimethyl Diazomalonate with Cyclohexene

Catalyst (mmole)	(16)	(18)	(17)	Total Product
0.0042	10.98 (1.00)	3.91 (0.356)	1.43 (0.130)	16.32
0.0085	20.08 (1.00)	4.58 (0.228)	1.30 (0.065)	25.96
0.0170	22.74 (1.00)	4.82 (0.212)	2.54 (0.112)	30.10
0.0350	43.76 (1.00)	5.26 (0.120)	3.65 (0.083)	52.67
0.0700	55.77 (1.00)	7.43 (0.133)	4.72 (0.085)	67.92
0.1400	73.53 (1.00)	11.52 (0.157)	5.98 (0.081)	91.03
0.2800	69.24 (1.00)	16.35 (0.236)	6.99 (0.101)	92.58
0.5600	58.52 (1.00)	14.99 (0.256)	4.49 (0.077)	78.00
1.120	55.77 (1.00)	29.23 (0.524)	5.32 (0.095)	90.32
2.240	50.62 (1.00)	28.49 (0.563)	3.64 (0.072)	82.75
4.480	45.65 (1.00)	32.95 (0.722)	0.00	78.60

Table 7. Product Distribution and Yields as a Function of $\text{Cu}(\text{AcAc})_2$ Concentration in the Reaction of Dimethyl Diazomalonate with Cyclohexene

Catalyst (mmole)	(16)	(18)	(17)	Total Product
0.0042	6.55 (1.00)	0.51 (0.078)	0.87 (0.134)	7.93
0.0085	6.86 (1.00)	0.62 (0.090)	0.86 (0.125)	8.34
0.0170	51.48 (1.00)	7.18 (0.139)	4.63 (0.090)	63.29
0.0350	40.76 (1.00)	3.10 (0.076)	5.58 (0.137)	49.44
0.0700	71.47 (1.00)	7.93 (0.111)	6.19 (0.087)	85.59
0.1400	78.08 (1.00)	12.39 (0.158)	5.92 (0.076)	96.39
0.2800	69.24 (1.00)	19.57 (0.283)	6.44 (0.093)	95.25
0.5600	55.43 (1.00)	34.44 (0.621)	5.00 (0.090)	94.87
1.120	48.65 (1.00)	20.93 (0.430)	7.52 (0.154)	77.10
2.240	42.04 (1.00)	6.87 (0.163)	4.76 (0.113)	53.67
4.480	22.48 (1.00)	2.82 (0.125)	6.37 (0.284)	31.67

Employing catalysts of the type $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuX}$, we found the amount of C-H insertion (the triplet like behavior) relative to cyclopropanation increases as the leaving group ability of X increases (Table 8).^[39]

Table 8. Effect of Anion upon Yields and Product Distribution in the Reaction of Cyclohexene with Dimethyl Diazomalonate.

$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuX}$ 0.14 mmole	(16)	(18)	(17)
X = BF_4^*	59.55 (1.00)	7.25 (0.122)	8.09 (0.136)
I	74.23 (1.00)	12.88 (0.174)	7.42 (0.101)
Br	68.64 (1.00)	15.11 (0.220)	6.68 (0.097)
Cl	63.92 (1.00)	13.25 (0.207)	4.69 (0.074)
SCN	28.31 (1.00)	1.31 (0.046)	1.82 (0.064)
CN	41.53 (1.00)	0.81 (0.020)	0.92 (0.023)

*Concentration less than 0.14 mmole due to decomposition during transfer.

In addition when common anions were added to reactions involving tri-alkylphosphite copper(I) chloride and iodide, the decomposition of diazo compound was severely depressed.^[39] On the other hand, addition of fluoroborate ion to the same reaction mixtures had only slight effect (Table 9).

Such behavior is consistent with a displacement of anion in a pre-equilibrium or rate determining step. The distinction between these two steps can be made.^[45] The optimum catalyst concentration for standard runs occurs at 0.14 mmole catalyst per 50 ml of olefin, independent of olefin or catalyst (copper(I) halide-trialkylphosphite and $\text{Cu}(\text{AcAc})_2$). This is consistent with loss of nitrogen being rate

Table 9. Effect of Common Ion on the Reaction of Cyclohexene with Dimethyl Diazomalonate

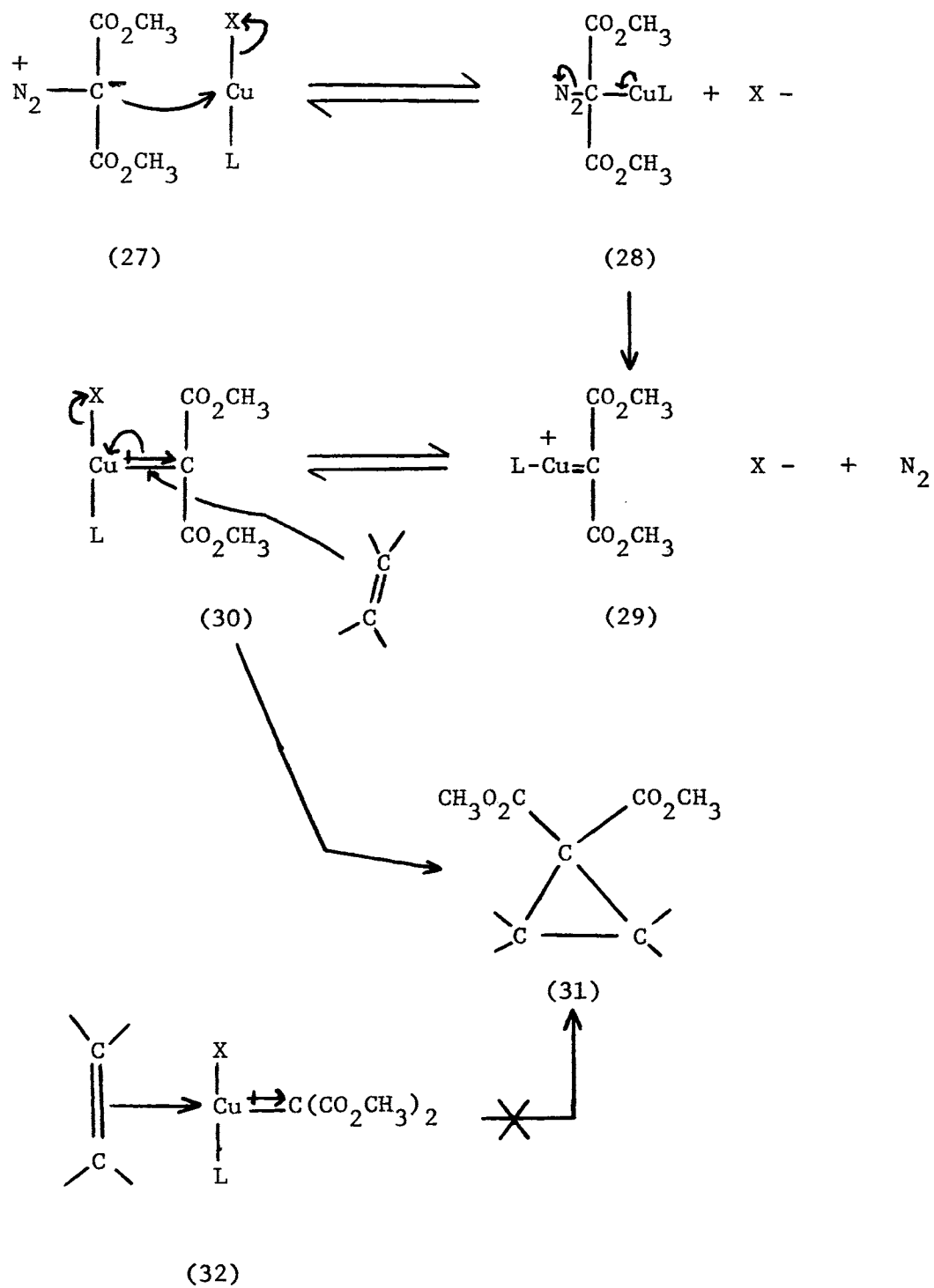
Catalyst	Salt	(16)	(18)	(17)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	none	74.23(1.00)	12.88(0.174)	7.42(0.101)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	$(\text{CH}_3)_4\text{NI}$	3.33(1.00)	0.00	7.08(2.12)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	$(\text{CH}_3)_4\text{NBF}_4$	63.66(1.00)	11.36(0.178)	5.00(0.078)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$	none	63.92(1.00)	13.25(0.207)	4.69(0.074)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$	$(\text{CH}_3)_4\text{NCl}$	8.58(1.00)	1.57(0.183)	0.00
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$	$(\text{CH}_3)_4\text{NBF}_4$	49.33(1.00)	5.26(0.107)	4.08(0.083)

determining and we therefore propose the mechanism shown in Scheme 4. This is a slight modification of that proposed by Moser.^[34,35]

Scheme 4

A necessary consequence of this mechanism and the partial rate data is the dependence of dimer formation upon the square of the concentration of the catalyst-carbene complex (30). In addition, the variation of the fumarate-maleate ratio over a range of concentrations, (Table 10) requires that a second path besides that shown in equation 4 be operative. This path depends upon the concentration of (27) and diazo compound (15). On steric grounds, fumarate will become increasingly dominant as path (30) becomes important.

In the case of ethyl diazoacetate, Moser^[46] reported the trialkylphosphite catalysts to be most effective with olefins which were carefully freed of peroxides. However, we did not find this to be the case. A positive peroxide effect is also observed in reactions of



Scheme 4

Table 10. Product Distribution in the Reaction of Cyclohexene with Ethyl Diazoacetate using $[(\text{CH}_3\text{O})_3\text{P}]_n \cdot \text{CuI}$ as Catalyst

Catalyst (mmole)	n	Norcarane			Cis	Dimer	
		exo	endo	ratio		Trans	Ratio
0.140	1	7.80	0.65	12.0	0.088	0.123	0.715
5.00	1	2.91	1.16	2.51	0.218	0.710	0.307
0.140	2	7.87	0.684	11.5	0.100	0.150	0.667
5.00	2	0.965	0.946	1.02	0.077	0.254	0.304
0.140	3	8.05	0.533	15.1	0.067	0.111	0.608
5.00	3	0.333	0.832	0.40	0.00	0.00	

dimethyl diazomalonate (Table 11).^[47,48] We have shown that treatment

Table 11. Effect of Peroxide upon the Reaction of Cyclohexene with Dimethyl Diazomalonate

Catalyst	Conditions	(16)	(18)	(17)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuI}$	A	74.23 (1.00)	12.88 (0.174)	7.42 (0.101)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuI}$	B	19.38 (1.00)	2.02 (0.104)	1.79 (0.092)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuI}$	C	72.02 (1.00)	11.35 (0.157)	5.28 (0.074)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuI}$	D	67.78 (1.00)	12.09 (0.178)	6.27 (0.093)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuBr}$	A	68.64 (1.00)	15.11 (0.220)	6.68 (0.097)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuBr}$	B	21.96 (1.00)	1.88 (0.086)	2.08 (0.094)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuBr}$	C	69.76 (1.00)	14.24 (0.204)	5.54 (0.080)
$(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuBr}$	D	67.35 (1.00)	11.77 (0.175)	5.46 (0.081)
None	C	9.44 (1.00)	1.83 (0.194)	0.00

- A. Untreated, commercial cyclohexene.
- B. Commercial cyclohexene filtered through alumina.
- C. Condition B, then benzoyl peroxide added.
- D. Condition B, then Vazo added.

of the catalyst with excess benzoyl peroxide furnishes copper(II) benzoate and we know from precedents that phosphites react with peroxides.^[49] The two processes are apparently competitive and we infer that we are generating copper(II) alkoxy halides.^[50] The presence of phosphite is inherently bad from the standpoint of carbenoid generation, for phosphites trap carbenes^[51] and generate phosphinazenes^[52] from diazo compounds. All of these factors were examined and we found that several additives grossly depressed yields (Table 12).^[39,53] In the case of copper(I) and (II) chlorides, the

Table 12. Effect of Additives upon Yields and Product Distribution in the Reaction of Cyclohexene with Dimethyl Diazomalonate using $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$ as Catalyst

Additive (30 mmole)	(16)	(18)	(17)
None	63.92 (1.00)	13.25 (0.207)	4.69 (0.074)
CuCl	33.46 (1.00)	33.44 (1.00)	2.29 (0.071)
$(\text{CH}_3\text{O})_3\text{P}$	46.07 (1.00)	21.18 (0.460)	3.75 (0.082)
$(\text{CH}_3\text{O})_3\text{PO}$	68.13 (1.00)	16.23 (0.238)	5.92 (0.087)
$(\text{CH}_3\text{O})_2\text{CH}_3\text{PO}$	60.58 (1.00)	19.20 (0.317)	5.08 (0.084)
$[(\text{CH}_3)_2\text{N}]_3\text{P}$	49.94 (1.00)	24.28 (0.486)	4.61 (0.092)
$[(\text{CH}_3)_2\text{N}]_3\text{PO}$	45.82 (1.00)	17.34 (0.378)	3.72 (0.081)
CuCl_2	55.00 (1.00)	17.96 (0.326)	5.34 (0.097)
$(\text{CH}_3\text{O})_2\text{HPO}$	59.54 (1.00)	25.14 (0.422)	4.48 (0.077)

effects may well result from the common ion effect. With phosphite esters we found that the resulting phosphinazenes do not generate carbenes

upon catalytic decomposition as is the case with phosphinazenes derived for diphenyldiazomethane, [54]

We have found the catalytic activity of $\text{Cu}(\text{AcAc})_2$ is completely independent of the presence or absence of peroxides (Table 13). Thus,

Table 13. Effect of Peroxides upon the $\text{Cu}(\text{AcAc})_2$ Catalyzed Addition of Dimethyl Diazomalonate to Cyclohexene²

Cyclohexene	(16)	(18)	(17)
Commercial	78.1	12.4	5.92
Peroxide free	78.5	12.4	5.81

we believe that copper(II) is the active catalyst species or is at least superior to copper(0) and copper(I).

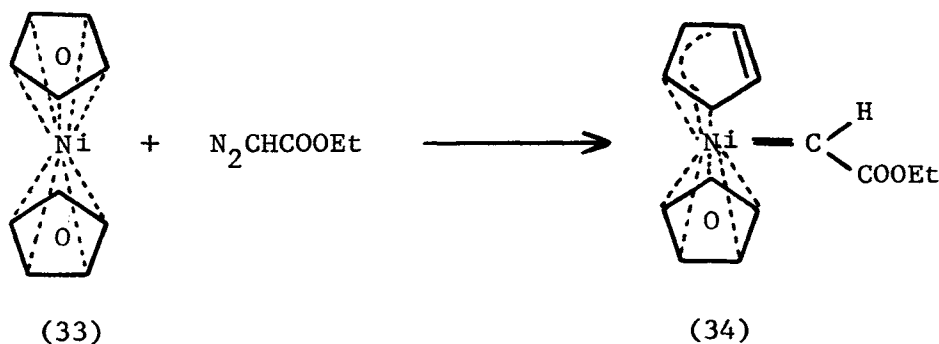
The correlations reported above with "copper(I)" catalyst are valid as are the resulting conclusions. This results from the rather fortuitous circumstance that we operated with single batches of olefin when performing comparison studies. Ironically, if we had employed Moser's precautions, it is doubtful that we would have made any of our observations and probably would not have undertaken these studies. His reaction conditions are sufficiently close to maximum catalyst solubilities that optimization and examination of catalyst concentrations over a range proportionally broad as our own would not have been possible.

In retrospect, the catalyst species most probably contributing to our results is an undefined copper(II) alkoxy halide. Fortunately sufficient peroxy impurities were always present to insure attaining

optimum conditions. This conclusion is not particularly unreasonable because the amount of catalyst (0.14 mmoles) is present in about 500 mmoles of olefin. Thus, a peroxide content of only 0.03 percent will furnish sufficient alkoxy radicals to convert all catalyst present to the copper(II) species.

3. Nickel Complexes

Nickelocene (33) shows marked selectivity toward diazo compounds. Werner and Richards^[55] found that addition of nickelocene to solutions



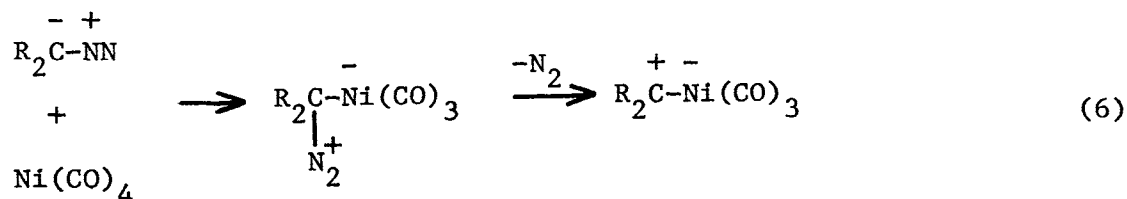
of diazomethane caused instantaneous nitrogen evolution and polymer formation. Even in the presence of cyclohexene, only polymer was formed. Nickelocene brings about rapid decomposition of diazopropene and ethyl diazoacetate formed cyclopropyl products when the reactions were carried out in olefins. The action of nickelocene appears to be catalytic; almost quantitative recovery of the nickelocene was made after some of the reactions.

Werner and Richards assumed that the failure of nickelocene to decompose diphenyldiazomethane and diazofluorene was due to steric factors. It appears that some other property of aromatic diazo compounds, such as the extent of charge delocalization, may also be involved.

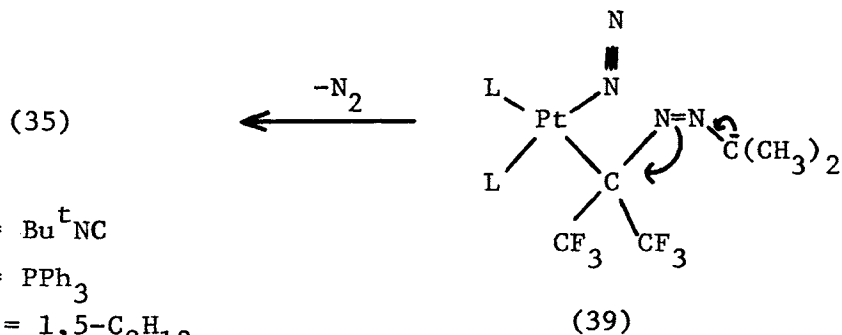
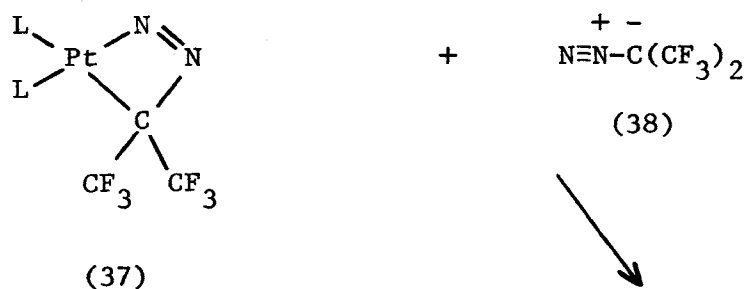
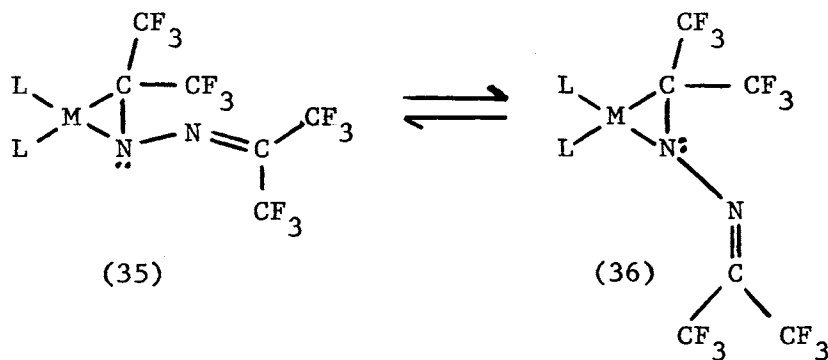
The steric consequences of the nickelocene catalyzed decomposition of ethyl diazoacetate are unusual. For example, cyclohexene gave fumarate, maleate and norcarane in the ratio 1.4:2.6:1.0. This is in contrast to copper catalyst which normally gave higher yields of the more stable fumarate dimer (vide supra). It should be noted, however, that the reactions were carried out by adding the catalyst to a solution containing all of the diazo compound, a condition which greatly favors dimer and azine formation. The synthetic utility of the reaction could probably be improved by slow, reverse addition. Werner and Richards explained the effect of nickelocene in terms of a complex having the "carbene" double bond directed toward the nickel atom. (34)

Nickelocene and $\text{Cu}(\text{AcAc})_2$ gave almost identical results in the addition of α -diazoacetophenone to vinyl acetate. [15]

Nickel carbonyl is an effective catalyst for decomposing most diazocompounds. The effect of nickel carbonyl was shown to be greater than that of the corresponding carbonyls of iron, cobalt, and molybdenum. [56] The reaction of ethyl diazoacetate with cyclohexene under the influence of nickel carbonyl yields only fumarate and norcarane, in a 6.1:1.0 ratio. [55] This is in sharp contrast to the effect of nickelocene and obviously reflects in part the different hybridizations and valence states of the metal atom. Mechanistically, the effect of metal carbonyl is probably similar to that of BF_3 . (Equation 6)



Bis (trifluoromethyl)diazomethane reacts with certain zero valence complexes of nickel, palladium and platinum to give complexes of type (35). These complexes are thought to arise through the intermediacy of (37) and (39).

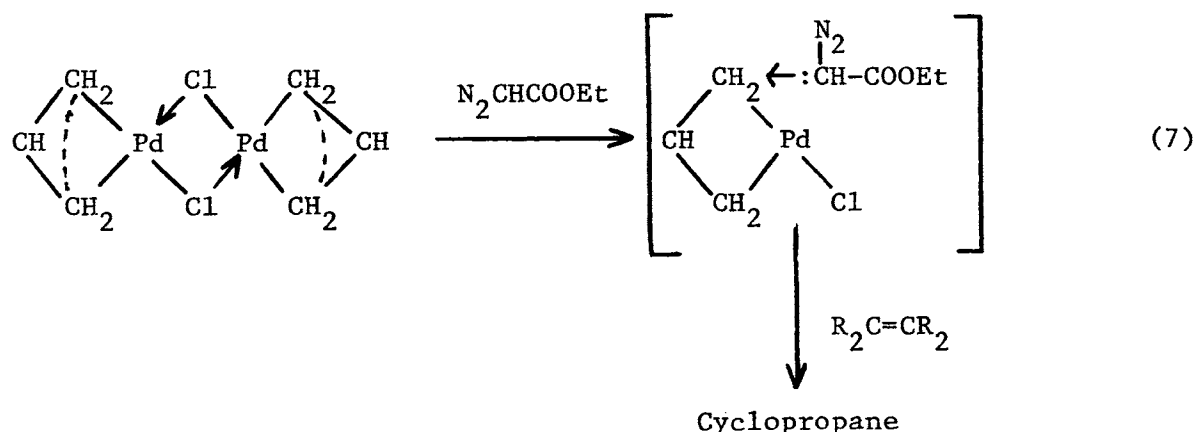


M = Ni, L = Bu^tNC
 M = Ni, L = PPh₃
 M = Ni, L₂ = 1,5-C₈H₁₂
 M = Pd, L = Bu^tNC
 M = Pd, L = C₆H₁₁NC
 M = Pt, L = PPh₃

4. Palladium Complexes

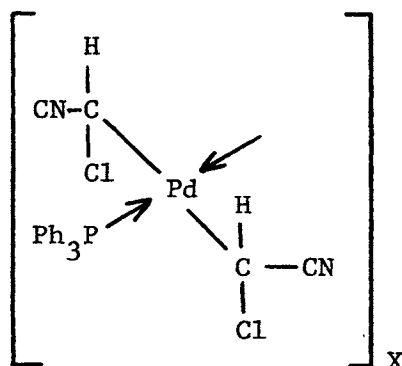
Armstrong has shown ethyl diazoacetate to be smoothly decomposed by di- μ -chlorodi- π -allyldipalladium at temperatures as low as 0 to 10°C. [58] Moderate to low yields of cyclopropanes result when the decomposition is carried out in the presence of olefins. The complex catalyzed the addition of only one carbene to dimethylacetylene, whereas copper gave the corresponding bicyclobutane.

Armstrong's work is of particular interest from a mechanistic standpoint. The palladium complex is known to be split by nucleophiles. [59] Thus, Armstrong assumed the first step of the reaction to be a nucleophilic attack by the diazo carbon on the complex, followed by elimination of nitrogen (Equation 7). This is similar to the mechanism suggested by Wulfman and Peace for trialkylphosphite copper(I) halides. [39]



The related dichloro-bis(triphenylphosphine)di- μ -chlorodipalladium also decomposes ethyl diazoacetate. [60] The norcarane was formed when the reaction was carried out in cyclohexene, but no mention was made of the yield or side reactions. Surprisingly, diazoacetonitrile reacted with the complex to give a stable complex (40) resulting from formal

insertion of the carbene into the Pd-Cl bond. This material is stable to 265°C. The corresponding palladium-cyclohexene complex, $(C_6H_{10}:PdCl_2)_2$, reacted in a similar manner, giving no norcarane.



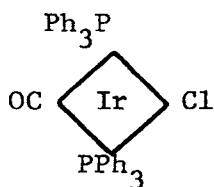
(40)

Palladium dichloride and di-chloro-di- π -allyldipalladium gave complexes with cyanocarbene, irrespective of the presence of cyclohexene. [60]

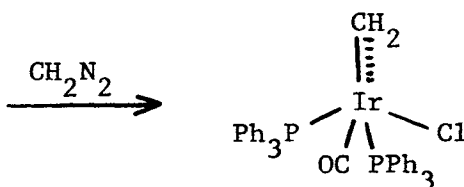
Bis(trifluoromethyl) diazomethane reacts with palladium chloride complexes to give Pd-Cl insertion products. [61]

5. Iridium Complexes

Iridium chlorocarbonylbis (triphenylphosphine) (41) [62] reacts with diazomethane to give a stable methylene containing complex (42). This complex will not transfer its methylene group to cyclohexene even



(41)



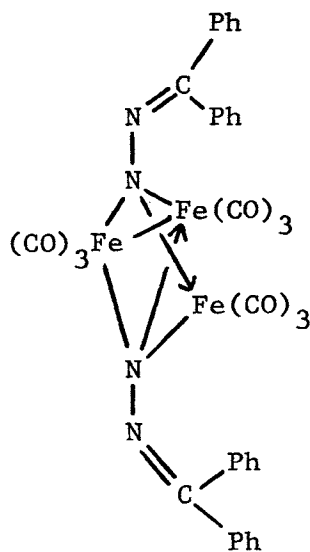
(42)

at 200°C. It does, however, react with the more polar double bond of styrene below 100°C.

6. Iron Complexes

Iron dipivaloylmethide has been used to decompose diazomethane in cyclohexene to give norcarane in low yield.^[63,64] Its behavior is similar to the usual behavior of copper and copper salts in that no C-H insertion products were formed. The complex was not destroyed during the reaction. Werner and Richards^[55] found ferrocene to have no effect on the thermal or photochemical reaction of diazomethane with cyclohexene.

An unusual reaction of diaryldiazomethane with iron carbonyl has been reported by Mills and coworkers.^[65,66] Diphenyldiazomethane does not decompose in the presence of pentacarbonyliron or dodecacarbonyltri-iron. A stable complex (43) was isolated which still contained the nitrogen atoms. Phenyldiazomethane failed to react. The utility of



(43)

the complex as a carbene precursor is doubtful since it is a high melting solid.

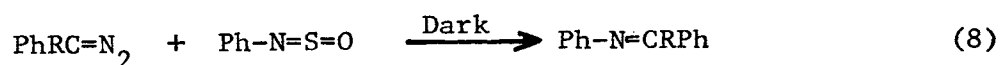
7. Chromium Complexes

Dicyclopentadienylchromium is unusual in that it does not react with diazomethane but does decompose ethyl diazoacetate.^[55] The complex reacts rapidly with one mole of diazoacetic ester but excess diazo compound is decomposed very slowly. Fumarate, maleate and norcarane are formed in a 1.5:0.6:1.0 ratio when the reaction is carried out in cyclohexene.

8. Miscellaneous

Stone et al.^[67,68] have reported on the reaction of bis(trifluoromethyl) diazomethane with several metal complexes. Stable carbene complexes were obtained from complexes of iron, cobalt, manganese, platinum, and iridium. Whether such complexes might be of use as catalysts to decompose other diazo compounds was not reported.

Stoffer and Musser^[69] have observed the unusual decomposition of diazo compounds by N-sulphinylaniline. Phenyldiazomethane and phenyldiazoethane react at room temperature in the dark with N-sulphinylaniline to give the corresponding ketimine. In contrast, diphenyldiazomethane underwent the reaction only under photolysis (Equation 8).



9. Conclusions

In reviewing the existing data on homogeneous catalyzed decompositions of diazo compounds, we conclude that the catalysis process up to the loss of nitrogen is strictly a Lewis acid-base phenomenon. After loss of nitrogen, back donation of low lying d-orbital electrons can stabilize the intermediate and lead to carbene like reactions. When no back donation is feasible (for energetic reasons or the absence of

d electrons) the reactions proceed in a fashion consistent with the character of the Lewis conjugate acid of the carbene, namely, carbonium ion character. Results with boron compounds support this contention. It should be possible to tailor catalysts to suit the unique requirements of a given reaction and diazo compound. We are currently engaged in attempts to clarify this point.

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CHAPTER III

ANGULAR ALKYLATION

ANGULAR ALKYLATION

One of the major problems in the total synthesis of terpenes and steroids is the stereospecific introduction of angular methyl groups or other carbon substituents. Reactions used or attempted in early work, namely alkylation with alkylhalides and conjugate addition of Grignard reagents,^{2,3} are relatively unsatisfactory because of their high sensitivity to steric hinderance giving predominantly the undesired cis product. Early successful efforts were based on the Robinson annelation⁴ process or various modifications,⁵ but this method is often plagued by low yields and impure products.⁶ Nagata et. al.^{7,8,9} introduced an improved hydrocyanation reaction using potassium cyanide and ammonium chloride. Later, alkylaluminum compounds^{10,11} were found to be superior co-reagents in the reaction. This process was recently used by Ireland and Welch¹² in the total synthesis of d,l-alnusenone.

The rearrangement of magnesium salts of halohydrins to ketones was recently used by Sistic and Vitale¹³ for the stereoselective cis introduction of an angular methyl group into trans-1-decalone.

(Figure 1)

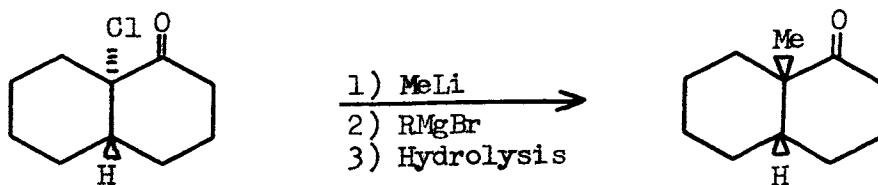


Figure 1

Storch and Stotter¹⁴ introduced an elegant synthesis of trans-fused, angularly substituted, polycyclic systems involving Diels-Alder addition to a dihydrothiophene. (Figure 2)

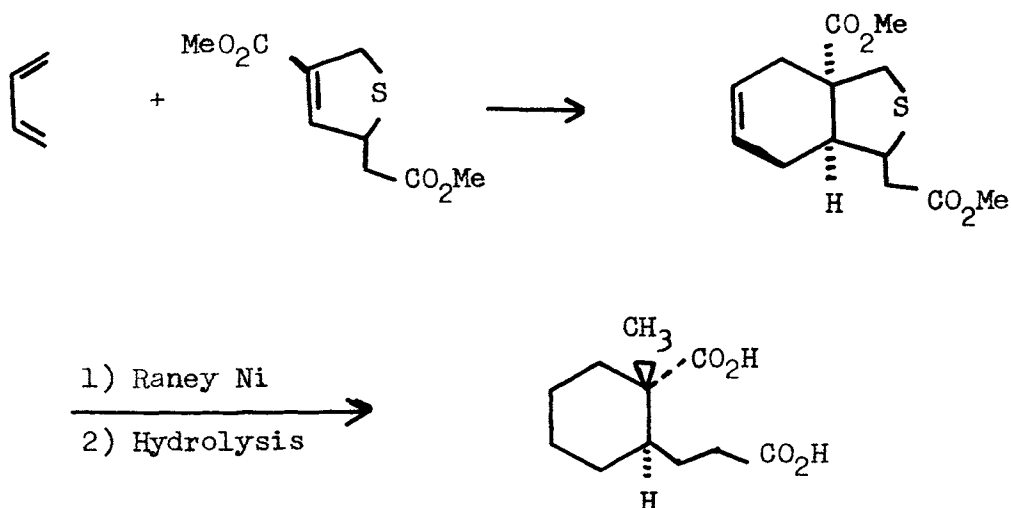


Figure 2

The literature contains numerous examples of angular methylation via cyclopropyl ring-opening.^{15,16,17} For example, Birch and co-workers utilized the following sequence (Figure 3) to introduce a

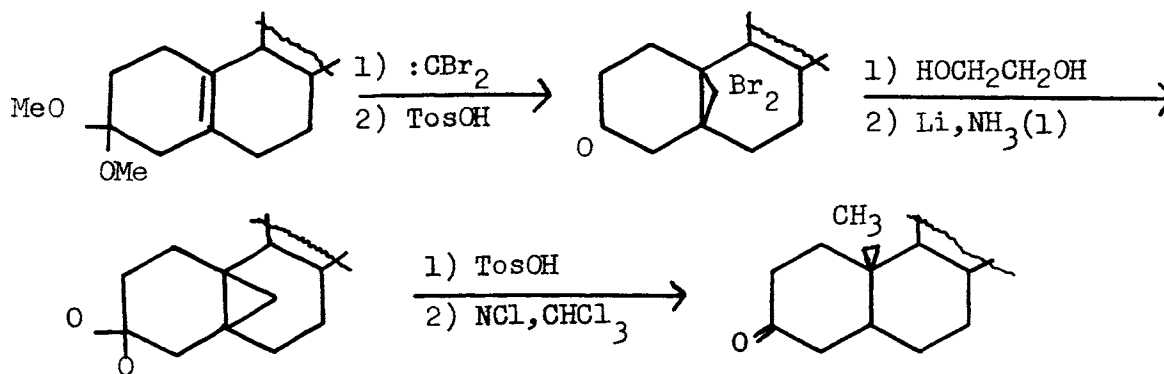


Figure 3

10-methyl group as part of the total synthesis of a non-aromatic steroid.

This method of angular methylation is particularly attractive in view of the fact that polar groups (OH, COOH, OCH₃) direct Simmons-Smith reagents cis to themselves.¹⁸ Sims¹⁹ used this fact to develop a synthetic sequence involving a stereospecifically formed cyclopropane ring and its subsequent selective opening to produce an angular methyl group. (Figure 4) In a non-steroid system, it has been shown that

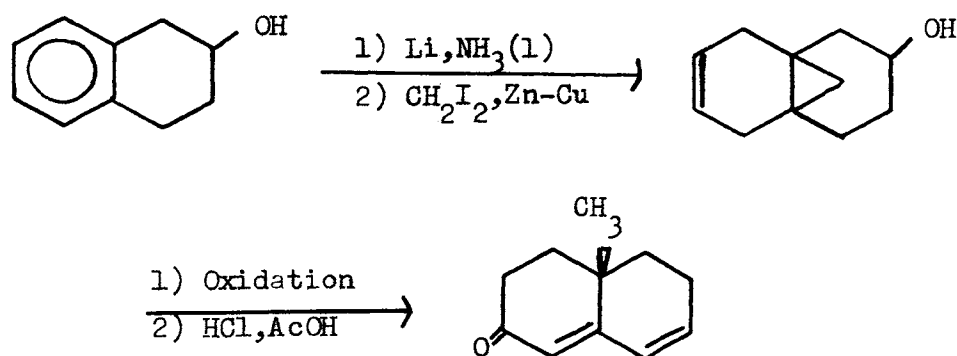


Figure 4

the acid function used to direct the Simmons-Smith addition can be removed during the ring-opening.²⁰ (Figure 5)

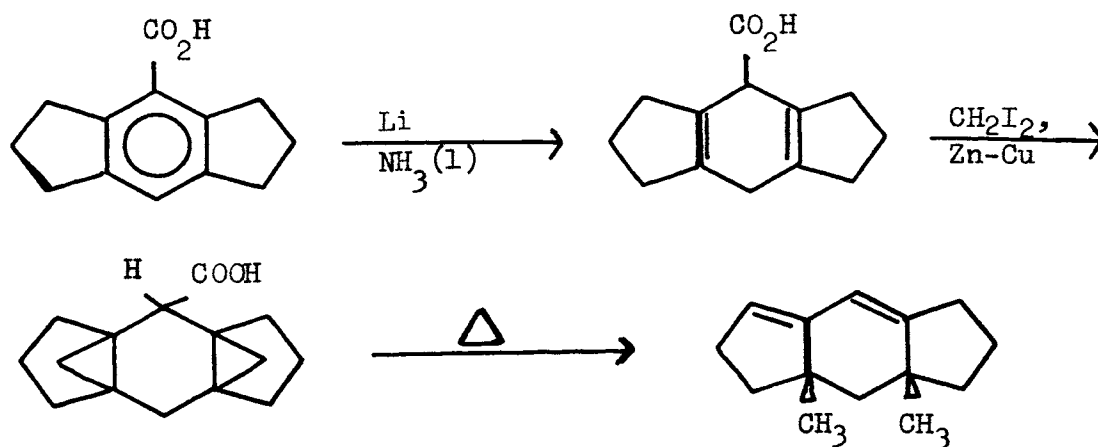


Figure 5

Several other examples of angular methylation via cyclopropanes are to be found in references 21-23.

Whitlock and Overman²⁴ have developed a potentially useful modification of the cyclopropane-angular methyl transformation. Thus, treatment of lithium enolates with Simmons-Smith reagent leads directly to the angular methylated product without isolation of the cyclopropyl adduct. (Figure 6)

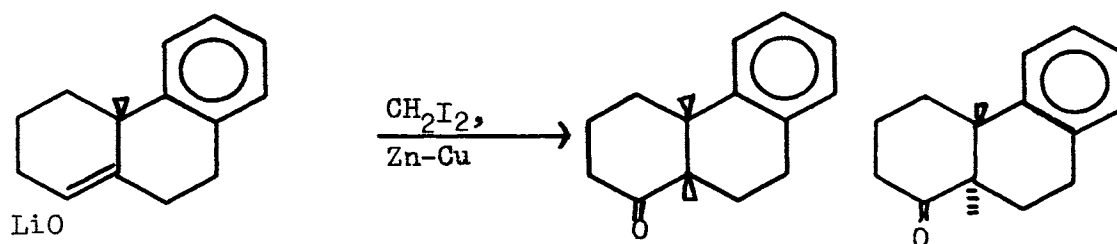


Figure 6

During a study of the stereochemistry of lithium dimethylcopper methylation, Marshall and Ruden²⁵ observed an unusual angular ethylation. Addition of the tricyclic enone to solutions of lithium dimethylcopper gave the ring-opened product in addition to the expected material. (Figure 7)

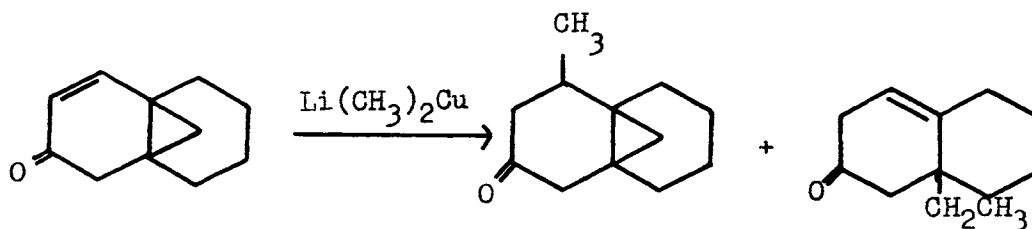


Figure 7

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CHAPTER IV

NUCLEOPHILIC CYCLOPROPYL RING-OPENING

NUCLEOPHILIC CYCLOPROPYL RING-OPENING

Spectroscopic evidence indicates considerable similarity between carbon-carbon double bonds and cyclopropyl systems.^{1,2} It is therefore, not surprising that a few properly substituted cyclopropanes are known to undergo nucleophilic reactions of the Michael type.³

In the condensation of ethylene bromide and diethyl malonate in the presence of sodium ethoxide, Bone and Perkin⁴ found that part of the initially formed cyclopropane dicarboxylate underwent further reaction with malonate anion to give the ring opened 1,1,4,4-tetramethoxycarbonylbutane. Thorpe and coworkers^{5,6,7} found that the reaction of 1-ethoxycarbonyl-1-cyanocyclopropane with either ethyl cyanoacetate or diethyl malonate gave ring-opened products. The ring-opened materials undergo further reactions yielding the corresponding cyclopentanoneimides. (Figure 1)

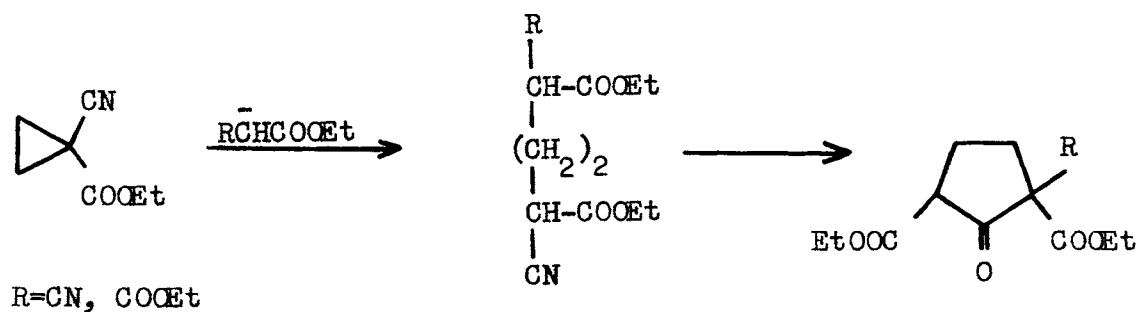


Figure 1

Ethyl sodiomalonate and 2-vinyl-1,1-diethoxycarbonylcyclopropane has been reported⁸ to react by attack at both the carbon-carbon double bond and the cyclopropane. (Figure 2)

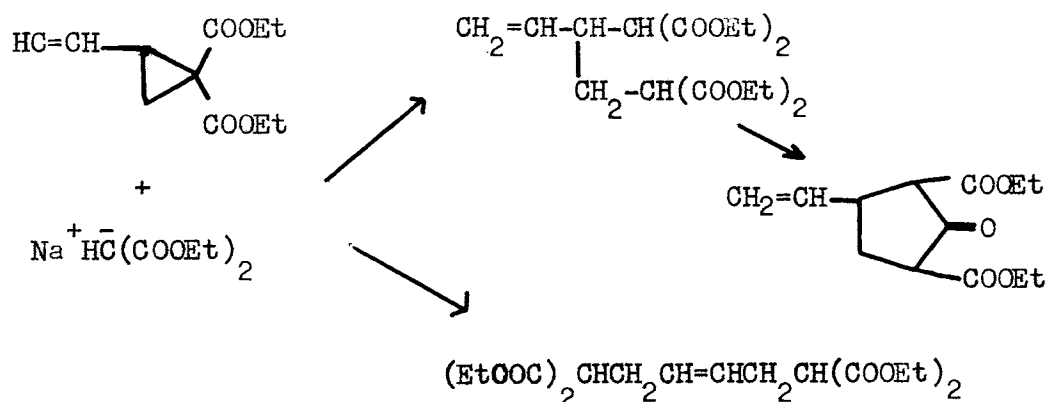


Figure 2

Bloomfield⁹ recently expressed some doubt as to the accuracy of this report. He was able to isolate only 2-3% of the ring-opened products using sophisticated distillation techniques. However, his studies were carried out using excess malonic ester as solvent, whereas alcoholic solvents were employed in the earlier work.

Stewart and Westberg¹⁰ have shown that secondary amines are effective nucleophiles for cyclopropyl ring opening, and Dolfini and coworkers¹¹ have shown that enamines can participate in the reaction. (Figure 3 and Figure 4)

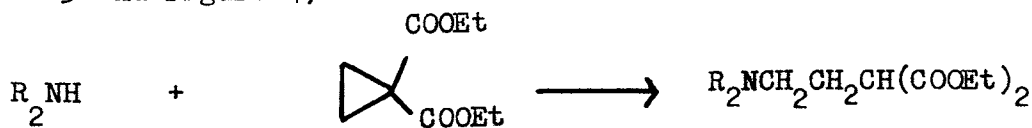


Figure 3

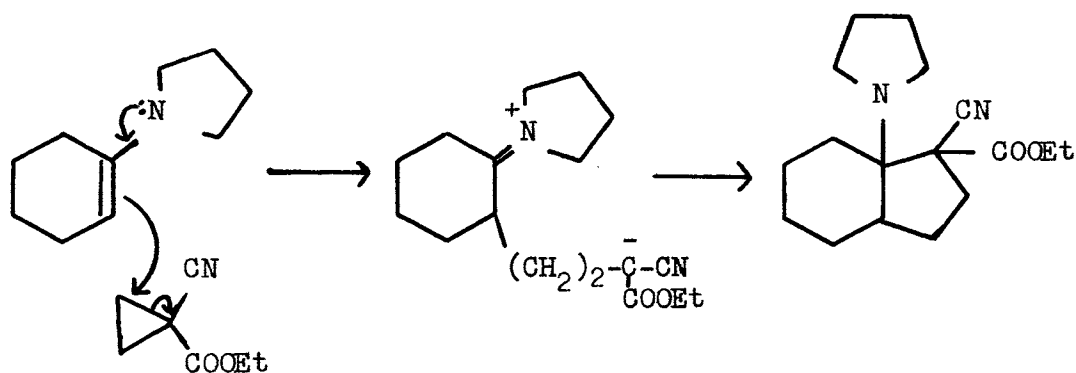


Figure 4

The anions from phenols, thiophenols and mercaptans also attack suitably substituted cyclopropanes in a similar fashion.¹⁰

The unusual dispiro-[5.0.5.1]-trideca-1,5,8,12-tetraone undergoes uncatalyzed ring-opening in the presence of alcohols or thiourea.¹²

(Figure 5)

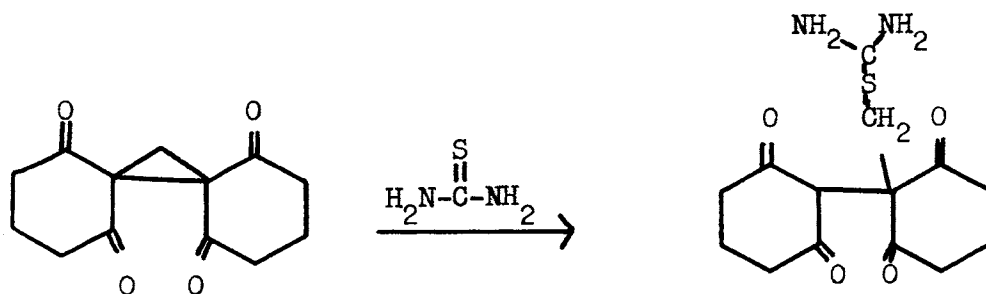
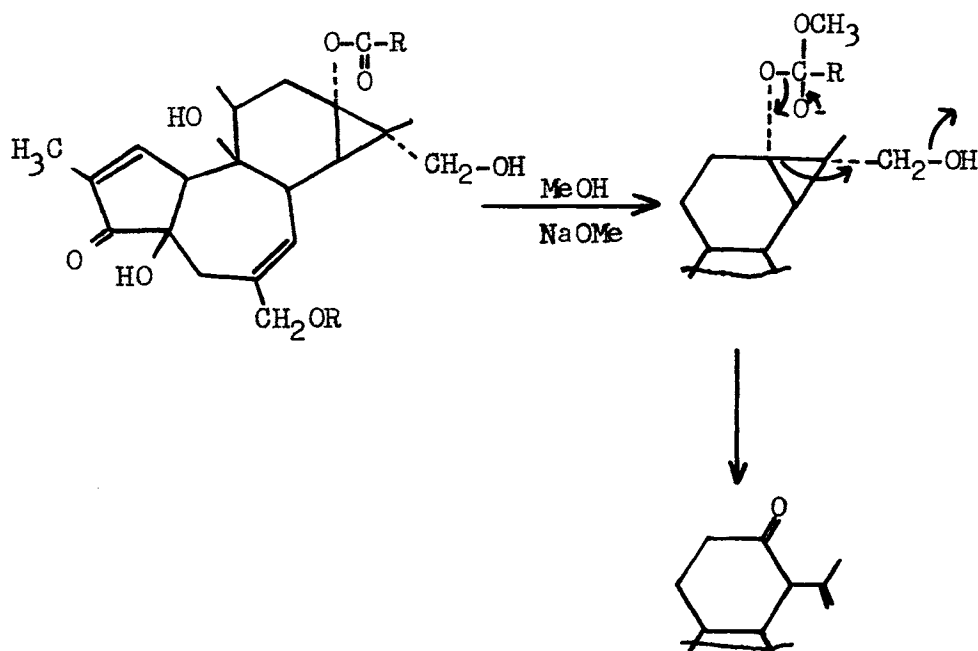


Figure 5

During the structure determination of tumor promoting phorbols, Gschwendt and Hecker¹³ observed an unusual cyclopropyl ring-opening and suggested the mechanism outlined in Figure 6.



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CHAPTER V
EXPERIMENTAL

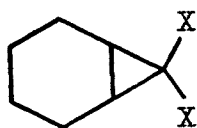
EXPERIMENTAL

Boiling points and melting points are given in degrees centigrade and are corrected. Spectra were determined on a Varian A-56/60 nuclear magnetic resonance spectrophotometer (n. m. r.) using tetramethylsilane as an internal standard and a Perkin-Elmer 337 infrared spectrophotometer using a polystyrene film as reference. Gas chromatographic (g.c.) analyses were performed using a Varian Aerograph model 90P and separations were carried out using a Varian Aerograph model A-700. All elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan. The term "solvent was removed" means by rotovaporation at water bath temperatures (75-90°C) unless otherwise stated.

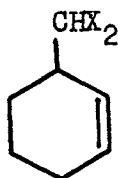
The dimethyl malonate, malonic acid, cyclohexene, 1-methylcyclohexene, cycloheptene, 3-methylcyclohexene, 3,5,5-trimethylcyclohexene, and 2-methylcyclohexanone employed were supplied by the Aldrich Chemical Co. Cis- and trans-2-heptene were supplied by the Chemical Samples Co. Cyclooctene and 1,3-cyclooctadiene were obtained from the Columbian Carbon Co. Trimethylphosphite was furnished by the Aldrich Chemical Co. All other phosphites were were generously given as samples by the Mobile Chemical Co. Copper salts were supplied by the Research Organic/Inorganic Chemicals Corp.

Before their use, all olefins were distilled and stored under nitrogen and over 4-A molecular sieves.

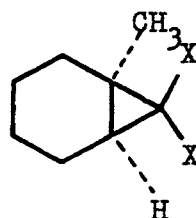
Through out the experimental and the results and discussion sections, the compounds below will be referred to by the corresponding Roman numerals.



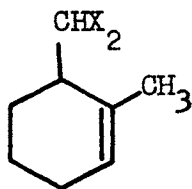
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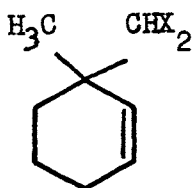
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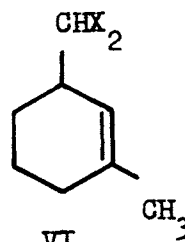
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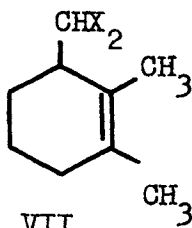
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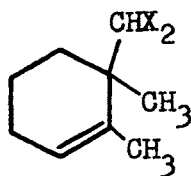
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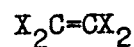
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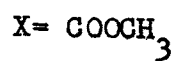
VII



VIII



IX



PREPARATION OF STARTING MATERIALS

The Preparation of p-Toluenesulfonyl Azide

p-Toluenesulfonyl azide was prepared by the method of Doering and DePuy.¹ To a mixture of 170 g (0.892 mole) of p-toluenesulfonyl chloride in 1 liter of 95% ethanol was added a solution of 70 g (1.08 mole) of sodium azide in 200 ml of water. The resulting mixture was stirred 2 hours at room temperature and poured into 6 liters of water. The oily azide settled out upon standing overnight. After decanting the aqueous layer, the azide was washed 3 times with 100 ml of water, once with 100 ml of saturated sodium chloride solution, dried over sodium sulfate and finally dried over calcium chloride. The yield was 150 g (86%) of colorless oily azide which was used without further purification. The reported yield was 82%. The infrared spectrum (neat) showed bands at 2110 (s, N_3), 1352 (s) and 1170 cm^{-1} (s,b) among others. The n. m. r. spectrum (CCl_4) had a singlet at τ 7.55, a doublet at τ 2.64 ($J=8cps$, H's ortho to the methoxy group) and a doublet at τ 2.22 ($J=8cps$).

The Preparation of Dimethyl Diazomalonate

A solution of 132 g (0.67 mole) of p-toluenesulfonyl azide, 71 g (0.70 mole) of triethylamine (which had been stored over potassium hydroxide pellets), and 93 g (0.70 mole) of dimethyl malonate in 600 ml of dry benzene was allowed to stand at room temperature overnight. The solid (p-toluenesulfonamide) was filtered and washed with 100 ml of cold benzene. The combined benzene solutions were concentrated in vacuo (water) using a 60°C water bath, and 200 ml of hexane was added to precipitate the remaining p-toluenesulfonamide. After removal of

the benzene-hexane solvent, the material was distilled to give 96.6 g (91%) of clear yellow oily dimethyl diazomalonate b.p. $42-44^{\circ}\text{C}/0.01\text{ mm}$ (lit. b.p. $63^{\circ}\text{C}/1\text{ mm}$).² The n. m. r. spectrum (CCl_4) showed the presence of 3-4% unreacted dimethyl malonate (the methyl ester hydrogen resonances of the diazo compound appear at $\tau 6.20$ and those of the unreacted malonate at $\tau 6.34$). The dimethyl malonate was removed by very slow distillation through a 6" column. The unreacted dimethyl malonate distilled over at $32-34^{\circ}\text{C}/0.01\text{ mm}$ and the dimethyl diazomalonate at $40-41^{\circ}\text{C}/0.01\text{ mm}$. In other runs it was found that the redistillation can be stopped after the dimethyl malonate is removed, as shown by the yellow color of the distillate. The infrared spectrum (neat) showed bands at 2130 cm^{-1} (s, $\text{C}=\text{N}_2$), 1740 and 1760 cm^{-1} (s, $\text{C}=\text{N}$), 1695 cm^{-1} (s, $\text{C}=\text{N}$), 1335 cm^{-1} (s,b). Analysis calculated for $\text{C}_5\text{H}_6\text{O}_4\text{N}_2$: C, 37.96; H, 3.80; N, 17.72. Found: C, 37.87; H, 3.79; N, 17.64.

The Preparation of Di-t-butyl Malonate

Di-t-butyl malonate was prepared by the method of Korst.³ A mixture of dry ethyl ether and 10 ml of concentrated sulfuric acid was placed in a 24 ounce ginger ale bottle, capped and placed in the freezer to cool. After cooling to -5°C , the bottle was opened and 100 g (0.96 mole) of malonic acid and 240 ml (3.0 mole) of isobutylene (also at -5°C) were added. The bottle was then recapped and let stand in the hood with occasional shaking until the malonic acid dissolved (about one day). The bottle was again cooled to -5°C , and the contents poured, with stirring, into a 3 liter beaker containing 150 g of sodium hydroxide in 500 ml of water and 500 g of ice. The mixture was transferred to a separatory funnel, the aqueous layer was drawn off and

extracted twice with ether. The ether extracts were combined with the organic layer, washed twice with 100 ml of water, twice with 50 ml of saturated sodium carbonate solution, once with 100 ml of saturated sodium chloride and finally dried over anhydrous sodium carbonate. The ether was removed and crude ester distilled from alkali washed glassware to yield 117 g (57%) of colorless di-*t*-butyl malonate, b.p. 62-63°C/1 mm (lit. b.p. 65-67°C/1 mm). Korst reported a 64% yield. The infrared spectrum (neat) showed bands at 2940 (s, C-H), 1740 (s,b, C=O), and 1143 cm^{-1} (s,b) among others. The n. m. r. spectrum (CCl_4) showed a singlet at τ 8.55 (18H) and a singlet at τ 6.94 (2H).

The Preparation of Di-*t*-butyl Diazomalonate

A solution of 54 g (0.25 mole) of di-*t*-butyl malonate, 25 g (0.25 mole) of triethylamine and 48 g (0.25 mole) of *p*-toluenesulfonyl azide in 500 ml of dry benzene was allowed to stand at room temperature for 4 weeks. The diazo compound was worked up as previously described for the dimethyl analogue to yield 60 g (98%) of material boiling at 40-50°C/0.01 mm. On slow redistillation, 25 ml of unreacted ester was recovered (b.p. 34-36°C/0.01 mm) and 28.5 g (47%) of the yellow di-*t*-butyl diazomalonate (b.p. 38-40°C/0.01 mm) was collected. The n. m. r. spectrum (CCl_4) showed a sharp singlet at τ 8.50 as the only peak. The infrared (neat) showed bands at 2130 cm^{-1} (s, $\text{C}=\text{N}_2$), 1725 and 1750 cm^{-1} (s, C=N). Analysis calculated for $\text{C}_{11}\text{H}_{18}\text{O}_4\text{N}_2$: C, 54.51; H, 7.45; N, 11.62. Found: C, 54.66; H, 7.26; N, 11.48.

The Preparation of 1,2-Dimethylcyclohexanol

A Grignard reagent was prepared by adding a solution of 113.4 g (0.93 mole) of methyl iodide in 200 ml of anhydrous ether to 22.6 g

(0.93 mole) of dry shiny magnesium turnings plus a crystal of iodine in 200 ml of anhydrous ether at a rate just fast enough to maintain gentle refluxing. After addition of methyl iodide was complete, the mixture was refluxed an additional hour, then cooled in an ice bath. A solution of 100.0 g (0.89 mole) of 2-methylcyclohexanone in 200 ml of anhydrous ether was then added over a period of 2 hours with stirring. When the addition was complete, the mixture was refluxed 1 hour. The reaction mixture was poured into a beaker of ice and the complex destroyed with concentrated hydrochloric acid and water. The organic layer was separated and the aqueous layer was extracted twice with 200 ml of ether. The combined organic solutions were washed with 100 ml of water, 50 ml of 5% sodium thiosulfate, 50 ml of 10% sodium bicarbonate, again with 50 ml of water, and finally washed with 100 ml of saturated sodium chloride and dried over sodium sulfate. Removal of the ether gave 120 g (94%) of the alcohol which was used without further purification. The infrared spectrum showed only a trace of unreacted ketone.

The Preparation of 1,2-Dimethylcyclohexene

1,2-dimethylcyclohexene was prepared by the method of Hammond and Nevitt.⁴ A crystal of iodine was added to 100 g of 1,2-dimethylcyclohexanol and the mixture distilled to give a mixture of olefins and water. The olefin layer was drawn off and the aqueous layer extracted twice with 50 ml of petroleum ether (30-60°C). The combined organics were washed once with 25 ml of water, once with 50 ml of saturated sodium chloride, then dried over sodium sulfate. After removal of the solvent, the liquid was distilled through a 4' spinning-band column.

Fractions were collected at 124-125°C (2-methylmethylenecyclohexane), 130-131.3°C (2,3-dimethylcyclohexene), and at 135.9-136.5°C (dimethylcyclohexene). A total of 75 g of the desired olefin was collected. G.c. analysis showed it to be 99% pure. Its n. m. r. spectrum (CCl_4) showed a broad peak centered at $\tau 8.09$ and a sharp singlet at $\tau 8.42$ (CH_3). Some of the ring protons lie under this last peak.

PREPARATION OF CATALYSTS

Trimethylphosphite Copper(I) Chloride

Method A. The procedure given here is a modification of the method of Arbuzov.^{5,6} A solution of 12.4 g (0.1 mole) of trimethylphosphite (which had been dried over metallic sodium) in 200 ml of dry benzene was stirred while 9.9 g (0.1 mole) of copper(I) chloride was added. Initially, the salt dissolved as rapidly as it was added, but some solid remained at the end of the addition. The unreacted salt was removed by filtration, the solvent was removed and 20 ml of methanol was added. The white crystals which formed were filtered and dried under vacuum (1 mm) at 50°C for 3 hours. The yield was 20.0 g (90%) of material melting at 192-193°C (lit.⁵ 190-192). In other runs using freshly prepared copper(I) chloride, the complex melted at 229-230°C. The higher melting complex was subjected to analysis. Analysis calculated for $C_3H_9O_3PCuCl$: C, 16.14; H, 4.03; Cl, 15.92; P, 13.90; Cu, 28.47. Found: C, 16.17; H, 3.95; Cl, 15.89; P, 14.04; Cu, 28.20.

Method B. This method was used by Beriger⁷ in the preparation of trimethylphosphite. A solution of 4.80 g (0.15 mole) of dry methanol in 50 ml of toluene was cooled to -10°C and 4.95 g (0.05 mole) of copper(I) chloride was added. With stirring, 6.53 g (0.05 mole) of phosphorus trichloride was added at a rate sufficient to maintain the temperature between -5 and -10°C. After the addition, the mixture was warmed to room temperature (20 minutes), during which time hydrogen chloride gas was evolved. The white solid was filtered off, washed

several times with cold pentane, then dried under vacuum (1 mm) at 50°C for 3 hours. The melting point of this complex was 194-196°C. The infrared spectrum (400-4000 cm^{-1}) was identical to that of the higher melting complex.

Method C. A solution of 12.4 g (0.1 mole) of trimethylphosphite in 100 ml of dry benzene was stirred as 6.7 g (0.05 mole) of copper(II) chloride was added. After 30 minutes at reflux, the mixture was filtered, cooled, and allowed to crystalize. A total of 10.0 g (90%) of trimethylphosphite copper(I) chloride melting at 194-196°C was collected. This material was identical to that prepared by methods A and B as shown by comparison of their infrared spectra (400-4000 cm^{-1}).

Trimethylphosphite Copper(I) Bromide

To a stirred solution of 7.20 g (0.05 mole) of trimethylphosphite in 50 ml of dry benzene was added 7.17 g (0.05 mole) of anhydrous copper(I) bromide. After 30 minutes at reflux, the mixture was filtered and the solvent removed. Methanol (20 ml) was added, and after cooling the crystals which formed were filtered and dried under vacuum (1 mm) at 50°C for 3 hours. A total of 11.7 g (88%) of complex melting at 226-228°C (lit.⁵ 180-182) was collected. Analysis calculated for $(\text{CH}_3\text{O})_3\text{P-CuBr}$: C, 13.47; H, 3.36; P, 11.58; Br, 29.88. Found: C, 13.16; H, 3.47; P, 11.61; Br, 29.94.

Trimethylphosphite Copper(I) Iodide

A solution of 7.20 g (0.05 mole) of trimethylphosphite in 50 ml of dry benzene was stirred as 9.55 g (0.05 mole) of copper(I) iodide was added. The mixture was heated for 30 minutes, then filtered hot

to leave 0.1 g of uncomplexed salt. The benzene was removed to give an oil with some suspended solid in it. Upon addition of methanol, the oil solidified. After cooling, the solid was filtered off, washed several times with cold methanol, then dried under a 1 mm vacuum at 50°C for 3 hours. The yield of material melting at 192-193°C (lit.⁸ 192-193) was 14.1 g (84%).

Trimethylphosphite Copper(I) Cyanide

A solution of 7.20 g (0.05 mole) of dry trimethylphosphite in 50 ml of dry benzene was stirred as 4.48 g (0.05 mole) of copper(I) cyanide was added. The salt was completely dissolved after stirring at room temperature for 30 minutes. The material obtained upon removal of the solvent failed to crystallize during the usual work up and could not be induced to do so. All solvent was removed by brief, room temperature vacuum distillation; the oily complex was used without further purification. The yield was 10.9 g (80%).

Trimethylphosphite Copper(I) Thiocyanate

The complex was prepared by method A described above for the copper(I) chloride complex. The yield of white solid, m.p. 151-153°C, was 11.2 g (82%). Analysis calculated for $(\text{CH}_3\text{O})_3\text{P-CuSCN}$: C, 19.55; H, 3.70; P, 12.63; S, 13.04; N, 5.70. Found: C, 19.54; H, 3.87; P, 12.72; S, 13.04; N, 5.80.

Trimethylphosphite Copper(I) Fluoroborate

In 50 ml of dry benzene 1.24 g (0.01 mole) of trimethylphosphite and 4.29 g (0.01 mole) of copper(I) fluoroborate-tritoluene (generously supplied by an anonymous donor in the Central Research Laboratory, Monsanto Co.) were mixed and stirred briefly at room temperature. The

benzene was removed to give a slightly blue colored oil. Due to the instability of the fluoroborate salt, no effort was made to crystallize or otherwise purify the complex.

Bis-(Trimethylphosphite) Copper(I) Iodide

A solution of 2.48 g (0.02 mole) of trimethylphosphite in 20 ml of dry benzene was stirred as 1.90 g (0.01 mole) of copper(I) iodide was added. After 30 minutes at reflux, the solution was filtered, the solvent removed in vacuo, and methanol added. After cooling, the crystals which formed were collected and dried in the usual way. A total of 4.00 g (91%) of white crystals melting at 69-70°C (lit.⁵ 69-70) was collected.

Tris-(Trimethylphosphite) Copper(I) Iodide

A 3.72 g (0.03 mole) sample of trimethylphosphite and 1.90 g (0.01 mole) of copper(I) iodide were allowed to react as described above for the 2:1 complex. After removal of the benzene, an oil remained which did not solidify upon addition of 20 ml of methanol. The complex did crystallize after standing overnight at 0°C. The white solid was filtered, washed several times with cold methanol and dried under vacuum (1 mm) at 50°C for 3 hours. The yield was 4.72 g (84%) of material melting at 118-119.5°C. Analysis calculated for $[(CH_3O)_3P]_3^+CuI$: C, 19.2; H, 4.80; I, 22.6; P, 16.5; Cu, 11.3. Found: C, 19.05; H, 4.80; I, 22.70; P, 16.40; Cu, 11.46.

Triphenylphosphite Copper(I) Bromide

A solution of 3.10 g (0.01 mole) of triphenylphosphite in 20 ml of dry benzene was stirred as 1.44 g (0.01 mole) of copper(I) bromide

was added. The mixture was stirred until all the salt dissolved, (one hour). The benzene was removed and 15 ml of ether added (addition of methanol immediately gave the odor of trimethylphosphite) to dissolve the resulting oil. A seed crystal was obtained on a porous plate and added to the cooled ether solution. The crystals which formed were collected and dried to give 3.20 g (91%) of material melting at 91-92°C (lit.^{5,9} 90.5-91.5).

Triphenylphosphite Copper(I) Iodide

A mixture of 6.20 g (0.02 mole) of triphenylphosphite and 3.82 g (0.02 mole) of copper(I) iodide in 50 ml of dry benzene was heated at reflux for 30 minutes. The mixture was filtered to give 1.91 g (50%) of unreacted copper salt. The solvent was removed and the resulting oil taken up in 20 ml of ether. The crystals which formed were collected and dried to yield 7.91 g (98%) of material melting at 73-75°C. This is the melting point reported⁵ for the bis-complex. No further effort was made to prepare the mono complex.

Tricyclohexylphosphite Copper(I) Bromide

A solution of 15.0 g (0.15 mole) of freshly distilled cyclohexanol in 100 ml of dry toluene was cooled to -10°C, and 7.18 g (0.05 mole) of copper(I) bromide was added. With stirring, 13.6 g (0.05 mole) of phosphorous tribromide was added at a rate designed to maintain the temperature below -5°C. When the addition was complete, the mixture was allowed to warm to room temperature and stirred an additional 20 minutes. Cold pentane was added to decrease the solubility; the solid was filtered off and washed several times with pentane. A dam was placed on the filter and the material evacuated for one hour to remove

pentane and hydrogen bromide. The solid was then dried in a 35°C vacuum oven at 1mm. The complex did not melt but decomposed at 60°C. It also decomposed upon standing at room temperature overnight.

Triisopropylphosphite Copper(I) Iodide

The reaction was carried out exactly as described for the trimethylphosphite catalyst. After removal of the benzene, 20 ml of isopropanol was added and the mixture cooled. The white solid was filtered off and dried under vacuum (1 mm) at 50°C for 2 hours. The yield of material melting at 199.5-200°C (lit.⁶ 199-200) was 16.2 g (90%).

Oxidation of Trimethylphosphite Copper(I) Iodide

Method A. A mixture of 4.5 g (0.014 mole) of trimethylphosphite copper(I) iodide in 25 ml of benzene was warmed to 50°C and 3.39 g (0.014 mole) of benzoyl peroxide was added over a 2 hour period in small portions. During the addition the solution became a deep blue color, but never completely homogeneous. The mixture was cooled and the solid filtered off and dried under vacuum at 50°C for 2 hours. The blue solid melted at 190-205°C.

Method B. A solution of 3.60 g (0.025 mole) of trimethylphosphite in 50 ml of dry benzene was treated with 4.77 g (0.025 mole) of copper(I) iodide as described earlier. The hot solution of the complex was immediately treated with 4.05 g (0.025 mole) of benzoyl peroxide in small portions over a period of 2 hours. Late in the addition a solid formed. After all of the peroxide had been added, the mixture was cooled and the blue solid filtered off. The solid melted at 243-249°C. A part of the material was transferred to a soxhlet extractor and

extracted for 24 hours with hexane. After drying, the sample melted at 258-262°C. Elemental analysis of the extracted solid showed the absence of phosphorus and iodine. The infrared spectrum was similar but not identical to that of copper(II) benzoate.

Oxidation of Copper(I) Iodide

A 4.77 g (0.025 mole) sample of copper(I) iodide was placed in 50 ml of dry benzene at 50°C and 4.05 g (0.025 mole) of benzoyl peroxide added in small portions over a 2 hour period. The solvent immediately assumed the characteristic color of iodine. When the addition was complete, the solid that had formed was filtered off and washed free of iodine with cool benzene. The solid melted at 279-281°C. Its infrared spectrum (KBr) was very similar to that of copper(II) benzoate. The reported melting point of copper(II) benzoate is 280-282°C.¹⁰

The solid was insoluble in most organic solvents, but a small amount was dissolved in refluxing tetrahydrofuran. After crystallization the material was brilliant blue in color and melted at 285-286°C. Analysis of this material indicated complexation of the salt with tetrahydrofuran. Analysis calculated for $C_{14}H_{10}O_4Cu \cdot C_4H_8O_2$: C, 54.92; H, 4.57. Found: C, 55.89; H, 4.57.

REACTIONS INVOLVING DIAZOMALONIC ESTERS

Tetramethoxycarbonylethylene

A solution of 0.5 g (2.20 mmole) of trimethylphosphite copper(I) chloride in 50 ml of benzene was heated at reflux while a solution of 15.8 g (0.1 mole) of dimethyl diazomalonate in 50 ml of benzene was added at the rate of 6 drops per minute. Nitrogen evolution stopped within 4 hours after the addition of diazo compound was completed. The mixture was filtered, the benzene removed, and the solid taken up in hot methanol. After three recrystallizations from methanol, the white needles melted at 119-120°C (lit.¹¹ 119-120). The infrared spectrum (KBr) showed bands at 2940 and 2680 cm^{-1} (w, C-H), 1725 cm^{-1} (s, C=O) and 1645 cm^{-1} (w, C=C). The n. m. r. spectrum (CCl_4) showed a sharp singlet at τ 6.13 as the only peak. The yield was 10.1 g (77%).

1,1,2,2-Tetramethoxycarbonylethane

A solution of 19.8 g (0.15 mole) of dimethyl malonate and 32 mg (0.14 mmole) of trimethylphosphite copper(I) chloride in 50 ml of benzene was heated at reflux while a solution of 15.8 g (0.1 mole) of dimethyl diazomalonate in 50 ml of benzene was added at the rate of 6 drops per minute. When nitrogen evolution ceased (about 6 hours), the mixture was filtered, the benzene removed, and the resulting oil taken up in methanol. On cooling, a solid was deposited which, after three recrystallizations from methanol, was pure white and melted at 136-137°C (lit.¹² 135). The infrared spectrum (CHCl_3) showed bands at 2960 cm^{-1} (w, C-H) and 1725 cm^{-1} (s, C=O). The n. m. r. spectrum showed a singlet at τ 6.22 (12H) and τ 5.83 (2H). On the basis of the above data, the compound was assigned the structure 1,1,2,2-tetra-

methoxycarbonylethane. The yield was 14 g (53%).

Addition of Dimethyl Diazomalonate to Cyclohexene

A 20 mg sample of trimethylphosphite copper(I) chloride (0.14 mmole) was dissolved in 25 ml of cyclohexene and the solution heated to reflux. A solution of 3.16 g (0.02 mole) of dimethyl diazomalonate in 25 ml of the same olefin was added at the rate of 6 drops per minute from a constant rate dropping funnel. After an additional 12 hours at reflux temperature, the excess olefin was removed. G.c. analysis was performed using a 5'x $\frac{1}{4}$ " SE-30 column under the following conditions: column temperature, 160°C; injector and detector temperature, 210°C; helium flow rate, 30 ml per minute. The residue showed the presence of four compounds. Comparison of g.c. retention times showed the major component to be 7,7-dimethoxycarbonylnorcarane. Two of the other compounds were identified by the same method, as tetramethoxycarbonylethylene and 1,1,2,2-tetramethoxycarbonylethane. The fourth component was identified as dimethyl (3-cyclohexenyl)malonate (II) by independent synthesis and comparison of g.c. retention times.

Synthesis of Dimethyl (3-Cyclohexenyl)malonate

A solution of 16.1 g (0.1 mole) of 3-bromocyclohexene,¹³ 13.2 g (0.1 mole) of dimethyl malonate and 5.4 g (0.1 mole) of sodium methoxide in 200 ml of anhydrous methanol was heated at 60°C for 12 hours. The solvent was removed to leave a mixture of salt (sodium bromide) and an oil. The oil was taken up in ether, the solution filtered and the ether removed. The slightly colored residue was distilled to give 22.0 g of colorless oil coming over at 68-71°C/0.01 mm. The n. m. r. spectrum (CCl_4) showed a multiplet centered at τ 4.34 (2H, vinyl), a

sharp singlet at τ 6.30 (6H, COOMe), a doublet centered at τ 6.77 (1H, malonyl), a multiplet centered at τ 7.17 (1H, substituted allylic position) and a broad multiplet centered at τ 8.34 (6H, ring protons). The infrared spectrum (neat) showed two carbonyl bands, 1725 and 1750 cm^{-1} and a band at 1645 cm^{-1} (w, C=C). The material was assigned structure II.

Addition of Dimethyl Diazomalonate to 1-Methylcyclohexene

A solution of 32 mg (0.14 mmole) of trimethylphosphite copper(I) chloride in 100 ml of 1-methylcyclohexene was heated at reflux while a solution of 31.6 g (0.2 mole) of dimethyl diazomalonate in 100 ml of the olefin was added at the rate of 6 drops per minute using a constant rate dropping funnel. When the addition was complete, reflux was continued for 12 hours. After removal of the excess olefin, the residue was distilled at 70-90°C/0.01 mm. On redistillation, 34.0 g of colorless oil was collected between 58-60°C/0.01 mm. G.c. analysis of the material showed the presence of four compounds and the n. m. r. spectrum showed vinylic character, although elemental analysis was correct for $\text{C}_{12}\text{H}_{18}\text{O}_4$. Analysis calculated for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C, 63.71; H, 8.01. Found for the mixture: C, 63.63; H, 8.00.

Relatively pure samples of each component were collected by preparative g.c. using a 20'x3/8" carbowax 20M column operating at 180°C.

Fraction A. This compound reacted rapidly with bromine in carbon tetrachloride and with potassium permanganate. Its n. m. r. spectrum (CCl_4) showed a broad multiplet centered at τ 4.50 (1H, vinyl), a sharp singlet at τ 6.32 (6H, COOMe), a broad multiplet centered at τ 6.92 (1H, malonyl), a broad undefined multiplet centered at τ 8.17 and over-

lapping another multiplet centered at τ 9.00 (10H total, ring and CH_3 protons). The infrared spectrum (neat) showed two carbonyl bands, 1725 and 1730 cm^{-1} , and a band at 1605 cm^{-1} (w, $\text{C}=\text{C}$). Analysis found: C, 63.42; H, 7.86. The compound was assigned the structure IV on the basis of the n. m. r. spectrum.

Fraction B. This compound required several minutes to show any reaction with bromine and with permanganate. The n. m. r. spectrum (CCl_4) showed a sharp singlet at τ 6.32 (6H, COOMe), and two broad overlapping multiplets between τ 7.59- 9.00 including a sharp singlet at τ 8.77. The total area between τ 7.59- 9.00 was 12H. The infrared spectrum (neat) showed a single carbonyl band at 1720 cm^{-1} and a band at 3050 cm^{-1} (w, cyclopropyl C-H). Analysis found: C, 63.20; H, 7.90. The compound was assigned structure III. Ozonolysis of the original reaction mixture further confirmed the assignment.

Fraction C. This material rapidly discolored both bromine in carbon tetrachloride and permanganate. The n. m. r. spectrum (CCl_4) showed a singlet at τ 4.54 (2H, vinyl), a singlet at τ 6.30 (6H, COOMe), a singlet at τ 6.67 (1H, malonyl) and two broad overlapping multiplets between τ 7.84 and τ 8.91, including singlets at τ 8.45, τ 8.65, and τ 8.80. The total area in the τ 7.84- 8.91 region was 9H. The infrared spectrum (neat) showed the split carbonyl, 1725 and 1730 cm^{-1} and a band at 1625 cm^{-1} (w, $\text{C}=\text{C}$). Analysis found: C, 61.73; H, 7.73. The compound was assigned structure V on the basis of the n. m. r. spectrum.

Fraction D. This material discolored both bromine and permanganate rapidly. The n. m. r. spectrum (CCl_4) showed a broad multiplet centered

at τ 4.79 (1H, vinyl), a singlet at τ 6.32 (6H, COOMe), a doublet centered at τ 6.92 (1H, malonyl, $J=8\text{cps}$), a broad multiplet centered at τ 7.17 (1H, substituted allylic position), and a broad multiplet centered at τ 8.34 (9H, methyl and ring protons). The infrared spectrum (neat) showed carbonyl bands at 1735 and 1750 cm^{-1} and a band at 1635 cm^{-1} (w, C=C). Analysis found: C, 63.67; H, 8.03. The compound was assigned structure VI on the basis of the n. m. r. spectrum.

Addition of Dimethyl Diazomalonate to 1,2-Dimethylcyclohexene

A 16 mg (0.07 mmole) sample of trimethylphosphite copper(I) chloride was added to 50 ml of 1,2-dimethylcyclohexene and the solution heated to reflux. A solution of 15.8 g (0.1 mole) of dimethyl diazomalonate in 50 ml of the same olefin was added at the rate of 6 drops per minute using a constant rate dropping funnel. At the end of the addition, reflux was continued for a total of 24 hours. The excess olefin was removed and the resulting oil distilled to give colorless oil distilling over at 70-80°C/0.01 mm. G.c. analysis of the material revealed the presence of two compounds and the n. m. r. spectrum showed vinyl character. Analysis calculated for $\text{C}_{13}\text{H}_{20}\text{O}_4$: C, 65.01; H, 8.34. Found (for the mixture): C, 65.02; H, 8.30.

Relatively pure samples of each component were obtained by preparative g.c. using a 20'x3/8" Carbowax 20M column operating at 180°C.

Fraction A. The material of shortest retention time rapidly discolored bromine in carbon tetrachloride and aqueous permanganate. Its n. m. r. spectrum (CCl_4) showed a multiplet centered at τ 4.60 (1H, vinyl), a doublet centered at τ 6.37 (6H, COOMe, $J=8\text{cps}$), a singlet at τ 6.50 (1H, malonyl), a singlet at τ 9.17 (3H, methyl) and a broad

multiplet between τ 7.67 and τ 9.00 from which a singlet rises at τ 8.44. The total area under the multiplet was 9H. The infrared spectrum (neat) showed two carbonyl bands, 1730 and 1745 cm^{-1} and a band at 1630 cm^{-1} (w, C=C). Analysis found: C, 64.35; H, 8.14. The material was assigned structure VIII on the basis of the n. m. r. spectrum.

Fraction B. The second fraction decolorized bromine and permanganate solution also. The n. m. r. spectrum (CCl_4) showed a doublet centered at τ 6.34 (6H, COOMe), a singlet at τ 6.50 (1H, malonyl) and a broad multiplet between τ 7.75 and τ 9.00 (13H, methyls and ring protons) including a sharp singlet at τ 8.40. The infrared spectrum (neat) showed a doublet in the carbonyl region, 1725 and 1745 cm^{-1} and a band at 1630 cm^{-1} (w, C=C). Analysis found: C, 64.11, H, 8.05. This material was assigned the structure VII on the basis of the n. m. r. spectrum.

Addition of Dimethyl Diazomalonate to Cycloheptene

A solution of 45 mg (6.14 mmole) of trimethylphosphite to copper(I) iodide in 25 ml of cycloheptene (which had been distilled from sodium) was heated at reflux while a solution of 3.16 g (0.02 mole) of the diazo compound in 25 ml of the olefin was added at the rate of 6 drops per minute from a constant rate dropping funnel. After 24 hours at reflux, the excess olefin was removed, the residue taken up in methanol, and filtered. G.c. analysis showed the presence of only one compound in addition to starting olefin. The methanol solution was cooled and the resulting solid recrystallized twice to give 3.62 g (80%) of material melting at 61-62°C. The infrared spectrum showed strong carbonyl absorption at 1720 cm^{-1} . The n. m. r. spectrum (CCl_4) showed

a doublet centered at τ 6.29 (6H, COOMe, $J=8$ cps) and an unresolved multiplet between τ 7.67 and τ 9.00 (12H, ring protons). Analysis calculated for $C_{12}H_{18}O_4$: C, 63.70; H, 7.96. Found: C, 63.09; H, 7.67.

A. Spang reported difficulty with this analysis due to sublimation.

On the basis of the above data, the compound was assigned the structure 8,8-dimethoxycarbonyl bicyclo[5.1.0] octane.

Addition of Dimethyl Diazomalonate to Cyclooctene

The reaction was performed as described for cycloheptene, except on a 0.05 mole scale. G.c. analysis of the crude reaction mixture showed only one new product. After removal of the excess olefin by distillation, the residue was taken up in methanol and allowed to crystallize. Two recrystallizations from methanol gave 11.6 g (78%) of white solid melting at 68-69°C. The infrared spectrum ($CHCl_3$) showed strong carbonyl absorption at 1715 cm^{-1} . The n. m. r. spectrum (CCl_4) showed a singlet at τ 6.29 (6H, COOMe) and unresolved absorption between τ 7.67 and τ 9.00 (14H, ring protons). Analysis calculated for $C_{13}H_{20}O_4$: C, 65.00; H, 8.33. Found: C, 65.00; H, 8.37. On the basis of the above data, the compound was assigned the structure 9,9-dimethoxycarbonyl bicyclo[6.1.0] nonane.

Addition of Dimethyl Diazomalonate to 3-Methylcyclohexene

The reaction was carried out exactly as described for the addition to cycloheptene. G.c. analysis of the crude reaction mixture showed a major component (85.5%), 6.42% dimer and 8.02% of material assumed to be insertion products. After removal of the excess olefin, the residual oil was distilled, the fraction between 72-75°C/0.01 mm being collected. The infrared spectrum (neat) showed strong carbonyl

absorption at 1720 cm^{-1} . The n. m. r. spectrum (CCl_4) showed a doublet centered at $\tau 6.29$ (6H, COOMe , $J=2\text{cps}$) and unresolved absorption between $\tau 7.67$ and $\tau 9.17$ (12 H, ring and Me protons) including a broad singlet at $\tau 8.44$. Analysis calculated for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C, 63.70; H, 7.96. Found: C, 63.80; H, 7.96. On the basis of the above data, the compound was assigned the structure 7,7-dimethoxycarbonyl-3-methylnorcarane. Two of the insertion products showed identical g.c. retention times as two products from addition of the carbene to 1-methylcyclohexene.

Addition of Dimethyl Diazomalonate to 3,5,5-Trimethylcyclohexene

The addition was carried out as previously described in the case of cycloheptene. A g.c. analysis of the crude product indicated a major component (91.70%), 8.30% of material assumed to be insertion products and the absence of any dimer. Distillation gave a water white liquid boiling at $83-89^\circ\text{C}/0.01\text{ mm}$. The n. m. r. spectrum showed a sharp doublet centered at $\tau 6.29$ (6H, COOMe , $J=2\text{cps}$) and unresolved absorption between $\tau 8.91$ and $\tau 9.91$ (16H, ring and Me protons). The infrared spectrum showed carbonyl absorption at 1720 cm^{-1} . Analysis calculated for $\text{C}_{14}\text{H}_{22}\text{O}_4$: C, 65.87; H, 8.65. Found: C, 65.92; H, 8.59. On the basis of the above data, the compound was assigned the structure 7,7-dimethoxycarbonyl-3,5,5-trimethylnorcarane.

Addition of Dimethyl Diazomalonate to Bicyclo[2.2.1] hepta-2,5-diene

The reaction was carried out in the usual manner. G.c. analysis of the crude reaction mixture showed it to consist of 70% dimer and 15% each of the two other products, assumed to be the endo and exo cyclopropanes.

Addition of Dimethyl Diazomalonate to 1,3-Cyclooctadiene

The addition was carried out as described for the addition of cycloheptene. After removal of the excess diene by distillation, g.c. analysis of the crude reaction mixture showed only one peak of high retention time. The residue was taken up in 20 ml of methanol and cooled. The crystals which formed were recrystallized three times from methanol to give 10.8 g of white solid melting at 59-60°C. The n. m. r. spectrum (CCl_4) showed a singlet at τ 4.37 (2H), a doublet centered at τ 6.82 (6H, $J=3\text{cps}$), and unresolved absorption between τ 7.37 and τ 9.10. Analysis calculated for $\text{C}_{13}\text{H}_{18}\text{O}_4$: C, 65.60; H, 7.56. Found: C, 65.33; H, 7.61. The above data did not distinguish between a 1,2- or 1,4-cyclo addition product.

Hydrogenation of Adduct from 1,3-Cyclooctadiene

A 5.0 g sample of the material, obtained from addition of dimethyl diazomalonate to 1,3-cyclooctadiene, was taken up in 100 ml of ethanol and hydrogenated at atmospheric pressure using a Joshel type hydrogenation apparatus using 5% Rh on alumina (1.20 g) as catalyst. The hydrogenation stopped when one mole of hydrogen had been consumed. The catalyst was removed, the solution concentrated to about 20 ml and the material allowed to crystallize. After recrystallization from ethanol, the hydrogenation product was shown to be identical to the product obtained by addition of the carbene to cyclooctene by comparison of m.p., infrared, and n. m. r. On the basis of the above data, the carbene addition product was assigned the structure 9,9-dimethoxycarbonyl bicyclo[6.1.0] nona-3-ene.

Addition of Dimethyl Diazomalonate to 1,2,3,4-Tetramethylbenzene

The addition was carried out exactly as described for olefins. After removal of the excess aromatic hydrocarbon, g.c. analysis showed the presence of 10 products. The oily residue was taken up in 20 ml of methanol and cooled. The crystals which formed were recrystallized three times from methanol. The g.c. trace of the pure product corresponded to one of the peaks of the g.c. taken of the crude material and accounted for 30% of the total yield. The n. m. r. spectrum of the white solid showed a singlet at τ 3.10 (1H, aromatic), a singlet at τ 5.23 (1H, malonyl), a singlet at τ 6.28 (6H, COOCH_3) and an unsymmetrical doublet at τ 7.77 (12H, Me). Analysis calculated for $\text{C}_{15}\text{H}_{20}\text{O}_4$: C, 68.23; H, 7.57. Found: C, 65.14; H, 7.21. A. Spang reported difficulty in this analysis due to sublimation. The solid melted at 94-96°C. The mass spectrum had a parent ion at 204 A. M. U. On the basis of the above data the compound was assigned the structure dimethyl 2,3,4,5-tetramethylphenylmalonate.

Preparation of 1-Methyl-7,7-dicarbomethoxynorcarane

A solution of 96 mg (0.42 mmole) of trimethylphosphite copper(I) chloride in 300 ml of 1-methylcyclohexene was heated to reflux in a 3-necked flask. With stirring, a solution of 158.2 g (1.0 mole) of dimethyl diazomalonate in 300 ml of the olefin was added at the rate of 6 drops per minute from a constant rate dropping funnel. When the addition was complete, reflux was continued overnight. The excess olefin was removed and the resulting oil taken up in 600 ml of ethyl acetate. The solution was cooled in a dry ice-acetone bath and excess ozone (Welsbach generator) bubbled through. While still cold, 300 ml of

acetic acid, 3 ml of concentrated hydrochloric acid and 100 ml of 3% hydrogen peroxide was added. This solution was allowed to warm, stand at room temperature for 24 hours, and was then poured into ice and neutralized with potassium hydroxide solution. After removal of the organic layer, the aqueous layer was extracted twice with 100 ml of ether. The combined organic layers were washed twice with 50 ml of water, twice with sodium bicarbonate solution (10%), again with water, and finally with 100 ml of saturated sodium chloride solution. After drying over sodium sulfate and removal of the solvents, the oil was distilled to give a water clear liquid boiling between 48-115°C/0.01 mm. On redistillation, the material distilled at 53-55°C/0.01 mm to give 100 g (43%) of the product. This material showed one peak in the g.c. The n. m. r. spectrum (CCl_4) showed a sharp singlet at $\tau 6.34$ (6H, COOCH_3) and a singlet at $\tau 8.80$ (CH_3). The ring protons appeared as two overlapping multiplets between $\tau 7.37$ and $\tau 9.14$ (12H). The infrared spectrum (neat) showed bands at 1725 cm^{-1} (s, C=O) and 3050 cm^{-1} (w, cyclopropyl C-H). Analysis calculated for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C, 63.71; H, 8.01. Found: C, 63.57; H, 8.00.

Preparation of 7,7-Di-t-butoxycarbonylnorcarane

A solution of 16 g (0.07 mmole) of trimethylphosphite copper(I) chloride in 50 ml of cyclohexene was heated to reflux, and a solution of 24.2 g (0.1 mole) of di-t-butyl diazomalonate in 50 ml of cyclohexene was dropped in at the rate of 6 drops per minute from a constant rate dropping funnel. After completion of the addition, reflux was continued overnight. After removal of the excess olefin, the oil was taken up in 20 ml of ethanol and cooled. The crystals which formed

were recrystallized three times from ethanol and dried. The yield of white solid melting at 82.5-83°C was 10.0 g (35%). The n. m. r. spectrum (CCl_4) showed a doublet centered at τ 8.54. The ring protons appeared as two broad, overlapping peaks between τ 7.54 and τ 9.00. The infrared spectrum (KBr) showed bands at 1710 cm^{-1} (s, C=O) and at 3050 cm^{-1} (w, cyclopropyl C-H). Analysis calculated for $\text{C}_{17}\text{H}_{28}\text{O}_4$: C, 68.94; H, 9.45. Found: C, 68.82; H, 9.49. On the basis of the above data, the material was assigned the structure 7,7-di-t-butoxycarbonylnorcarane.

Preparation of 1-Methyl-7,7-di-t-butoxycarbonylnorcarane

A solution of 64 mg (0.28 mmole) of trimethylphosphite copper(I) chloride in 300 ml of 1-methylcyclohexene was heated to reflux. With stirring, a solution of 121.0 g (0.5 mole) of di-t-butyl diazomalonate in 300 ml of the same olefin was added at the rate of 6 drops per minute using a constant rate dropping funnel. After the addition was complete, reflux was continued overnight. Upon removal of the excess olefin, the residue was taken up in 1200 ml of methanol and treated with excess ozone while cooled in a dry ice-acetone bath. While still cold, 50 ml of dimethyl sulfide¹⁴ was added to the solution. With out removing from the cooling bath, the solution was allowed to warm to room temperature. After three hours at room temperature, the solvent was removed, the residue taken up in 500 ml of 10% potassium hydroxide, and 50 ml of 40% hydrogen peroxide added.¹⁵ This solution was allowed to stand at room temperature for 18 hours, then extracted three times with ether. The ether solution was washed twice with water, once with saturated sodium chloride solution, then dried over anhydrous sodium sulfate. After removal of the solvent, the oil was distilled, the main

fraction coming over at $73-75^{\circ}\text{C}/0.01\text{ mm}$. On standing at room temperature, the colorless liquid partially solidified. The n. m. r. spectrum (CCl_4) showed a sharp singlet at $\tau 8.55$ (COOtBu) and a singlet at $\tau 8.85$ (CH_3). The ring protons appeared as two broad overlapping peaks between $\tau 7.45$ and $\tau 8.90$. The infrared spectrum showed bands at 1710 cm^{-1} (s, C=O) and 3050 cm^{-1} (w, cyclopropyl C-H). Analysis calculated for $\text{C}_{18}\text{H}_{30}\text{O}_4$: C, 69.62; H, 9.67; M.W., 310. Found: C, 69.24; H, 9.85; M.W., 319. On the basis of the above data, the compound was assigned the structure 1-methyl-7,7-di-t-butoxycarbonylnorcarane. The yield was 31 g (20%).

Preparation of Tetra-t-butoxycarbonylethylene

A solution of 0.5 g of trimethylphosphite copper(I) chloride in 50 ml of benzene was heated at reflux while a solution of 24.2 g (0.1 mole) of di-t-butyl diazomalonate in 50 ml of benzene was added at the rate of 6 drops per minute from a constant rate dropping funnel. Reflux was continued until nitrogen evolution ceased (about 3 hours). After filtering, the solvent was removed and the residual oil taken up in 20 ml of ethanol. On cooling, a solid was formed which recrystallized three times from ethanol to give 6.5 g of white crystals melting at $169-170^{\circ}\text{C}$. The infrared spectrum (KBr) showed bands at 2980 cm^{-1} (m) and 2940 cm^{-1} (w, C-H), 1740 and 1730 cm^{-1} (s, C=O), and 1640 cm^{-1} (w, C=C). The n. m. r. spectrum (DCCl_3) showed a singlet at $\tau 8.47$ as the only peak. Analysis calculated for $\text{C}_{22}\text{H}_{36}\text{O}_8$: C, 61.68; H, 8.40; M.W., 428. Found: C, 61.64; H, 8.53; M.W., (Chloroform) 428. On the basis of the above data, the compound was assigned the structure tetra-t-butoxycarbonylethylene.

Addition of Dimethyl Diazomalonate to Cis-2-heptene

The addition was carried out as previously described for cycloheptene using 96% pure cis-2-heptene. G.c. analysis of the crude mixture showed a major component, 95.6%, 3.36% carbene dimer and 0.52% each of two other compounds. The excess olefin was removed and the residue distilled, the fraction coming over at 60-63°C/0.05 mm being collected. The n. m. r. spectrum (CCl_4) of the colorless oil showed a singlet at τ 6.30 (6H, COOMe) and an unresolved multiplet between τ 8.05 and τ 9.22 (14H). Analysis calculated for $\text{C}_{12}\text{H}_{20}\text{O}_4$: C, 63.15; H, 8.77. Found: C, 63.13; H, 8.62. The compound was tentatively assigned the structure of the cis-cyclopropyl adduct.

Addition of Dimethyl Diazomalonate to Trans-2-heptene

The diazo compound was added to 99% pure trans-2-heptene in the manner previously described for cycloheptene. G.c. analysis of the crude reaction mixture showed a major component, 76.0%, 17.4% carbene dimer and two unresolved components accounting for 6.60% of the mixture. These last two products disappeared from the g.c. trace upon the addition of bromine to the reaction mixture and are, therefore, insertion products and not the cis-cyclopropane. After removal of the excess olefin, the residue was distilled to give a colorless oil distilling over at 58-60°C/0.05 mm. G.c. analysis of the distillate showed it to be pure and to be different from the adduct obtained from addition to the cis olefin. The n. m. r. spectrum (CCl_4) was similar to that of the cis adduct for the shape and positions of the individual peaks in the τ 8.05- τ 9.22 multiplet. Analysis calculated for $\text{C}_{12}\text{H}_{20}\text{O}_4$: C, 63.15; H, 8.77. Found: C, 63.00; H, 8.71. On the basis of the

g.c. and n. m. r. data, the cyclopropanes derived from the 2-heptenes were assigned the same configuration as their starting olefins.

CATALYSTS STUDIES

The effect of several catalysts on the addition of dimethyl diazomalonate to olefins (mainly cyclohexene and 1-methylcyclohexene) was studied with respect to the following variables: catalyst concentration, solvent, temperature, additives and peroxide content of the olefin. These data are presented in the following tables.

In all cases, the reactions were carried out as described below. All glassware was baked out overnight at 200°C, and assembled while hot. Olefins were distilled and stored over 4-A molecular sieves unless otherwise stated. Dimethyl diazomalonate was distilled to 99.9% purity as shown by n. m. r.

General Procedure. A 100 ml three-neck, round-bottom flask was equipped with a magnetic stirrer, reflux condensor, calcium chloride drying tube, and a constant rate dropping funnel. The catalyst was weighed in a glassine cup, carefully transferred to the flask and 25 ml of olefin added. The mixture was heated to the desired temperature with stirring. The diazo compound (0.02 mole) was dissolved in a second 25 ml portion of olefin, and added to the heated catalyst solution at the rate of six drops per minute (2.5 hours). Reaction was continued for a total of 24 hours. The reaction mixture was filtered while hot and excess olefin (or solvent) removed by distillation. The residue was taken up in the minimum amount of chloroform, 1 ml of triglyme was added (volumetric pipet) as an internal standard, and the mixture analyzed by glpc. Relative peak intensities were determined using a Beckman 10-inch ball and disc integrating recorder. The numbers in all tables represent percent yields based on available

diazo compound. The numbers in parenthesis are product distributions based on cyclopropane.

TABLE I

EFFECT OF CATALYST UPON YIELD IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENES

Catalyst	Cyclohexene			1-Methylcyclohexene					1,2-Dimethylcyclohexene		
	I	II	IX	III	IV	V	VI	IX	VII	VIII	IX
Cu	38.0	1.71	8.05	22.9	1.23	4.13	18.5	5.64	27.5	7.88	16.6
CuCl	42.8	2.18	8.38	19.1	1.45	3.67	17.5	4.83	27.5	7.44	22.4
CuSO ₄	45.3	2.08	9.07	24.8	2.49	6.07	24.0	7.36	16.0	5.55	21.9
(CH ₃ O) ₃ P-CuCl	63.7	4.67	18.4	29.6	2.30	10.7	26.0	5.15	32.8	10.4	19.5
(CH ₃ O) ₃ P-CuI	73.5	5.98	11.5								
Cu(AcAc) ₂	78.1	5.92	12.4								

TABLE II

PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ (METHOD A) CONCENTRATION
IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	36.21(1.00)	2.40(0.066)	3.19(0.089)	41.80
0.0085	40.24(1.00)	6.13(0.152)	3.60(0.092)	49.97
0.0170	43.67(1.00)	7.56(0.173)	4.47(0.092)	55.70
0.0350	67.44(1.00)	4.65(0.068)	5.36(0.086)	77.45
0.0700	68.21(1.00)	8.42(0.123)	5.49(0.092)	82.12
0.1400	46.08(1.00)	6.95(0.151)	4.16(0.091)	57.19
0.2800	49.85(1.00)	9.10(0.183)	4.80(0.096)	63.75
0.5600	62.55(1.00)	15.87(0.254)	6.16(0.099)	84.58
1.120	22.14(1.00)	31.96(1.44)	2.50(0.110)	56.60
2.240	7.59(1.00)	40.88(5.39)	1.39(0.184)	49.86
4.480	3.84(1.00)	53.51(13.9)	3.82(0.980)	61.17

TABLE III

PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ (METHOD B) CONCENTRATION
IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	8.11(1.00)	6.61(0.815)	0.00	14.72
0.0085	4.80(1.00)	7.51(1.56)	0.00	12.31
0.0170	40.67(1.00)	9.38(0.231)	3.19(0.078)	53.24
0.0350	43.76(1.00)	5.67(0.130)	3.14(0.072)	52.57
0.0700	35.18(1.00)	9.55(0.271)	2.68(0.076)	47.41
0.1400	63.92(1.00)	13.25(0.207)	4.69(0.074)	81.86
0.2800	61.77(1.00)	21.55(0.349)	5.32(0.086)	88.64
0.5600	33.81(1.00)	32.33(0.956)	2.33(0.069)	68.47
1.120	11.58(1.00)	19.07(1.65)	0.92(0.079)	31.57
2.240	7.38(1.00)	41.25(5.59)	5.30(0.718)	53.93
4.480	2.40(1.00)	33.20(13.8)	4.29(1.78)	39.89

TABLE IV

PRODUCTION DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ (METHOD C) CONCENTRATION
IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	6.74(1.00)	7.96(1.18)	0.00	14.70
0.0085	31.83(1.00)	13.13(0.412)	5.53(0.174)	50.49
0.0170	36.89(1.00)	7.73(0.209)	3.13(0.085)	47.75
0.0350	58.00(1.00)	5.83(0.100)	3.05(0.052)	66.88
0.0700	60.49(1.00)	9.56(0.158)	4.34(0.072)	74.39
0.1400	51.91(1.00)	14.62(0.282)	3.74(0.072)	70.27
0.2800	42.21(1.00)	43.11(1.02)	2.83(0.068)	88.15
0.5600	16.30(1.00)	66.15(4.06)	1.42(0.087)	83.87
1.120	13.47(1.00)	64.41(4.78)	1.26(0.094)	79.14
2.240	10.98(1.00)	61.94(5.94)	1.34(0.122)	74.26
4.480	8.03(1.00)	35.80(4.46)	3.76(0.467)	47.62

TABLE V

PRODUCT DISTRIBUTION AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuI}$ CONCENTRATION IN THE REACTION
OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	10.98(1.00)	3.91(0.356)	1.43(0.130)	16.32
0.0085	20.08(1.00)	4.58(0.228)	1.30(0.065)	25.96
0.0170	22.74(1.00)	4.82(0.212)	2.54(0.112)	30.10
0.0350	43.76(1.00)	5.26(0.120)	3.65(0.083)	52.67
0.0700	55.77(1.00)	7.43(0.133)	4.72(0.085)	67.92
0.1400	73.53(1.00)	11.52(0.157)	5.98(0.081)	91.03
0.2800	69.24(1.00)	16.35(0.236)	6.99(0.101)	92.58
0.5600	58.52(1.00)	14.99(0.256)	4.49(0.077)	78.00
1.120	55.77(1.00)	29.23(0.524)	5.32(0.095)	90.32
2.240	50.62(1.00)	28.49(0.563)	3.64(0.072)	82.75
4.480	45.65(1.00)	32.95(0.722)	0.00	78.60

TABLE VI
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $[(CH_3O)_3P]_2CuI$ CONCENTRATION OF THE
REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	6.21(1.00)	3.74(0.602)	0.90(0.145)	10.85
0.0085	6.02(1.00)	5.14(0.854)	0.91(0.151)	12.07
0.0170	5.36(1.00)	6.76(1.26)	0.94(0.176)	13.06
0.0350	4.69(1.00)	5.02(1.07)	0.41(0.088)	10.12
0.0700	2.78(1.00)	2.01(0.723)	1.39(0.500)	6.18
0.1400	65.80(1.00)	19.20(0.292)	6.58(0.100)	91.58
0.2800	56.71(1.00)	20.96(0.365)	5.10(0.090)	82.50
0.5600	56.63(1.00)	34.31(0.606)	5.49(0.097)	96.43
1.120	50.36(1.00)	28.61(0.568)	4.49(0.089)	83.47
2.240	34.31(1.00)	17.59(0.512)	3.34(0.100)	55.34
4.480	9.01(1.00)	27.75(3.08)	0.00	36.76

TABLE VII
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $[(CH_3O)_3P]_3-CuI$ CONCENTRATION OF THE
REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	7.25(1.00)	7.33(1.01)	6.61(0.910)	21.19
0.0085	15.87(1.00)	3.73(0.235)	1.06(0.068)	20.66
0.0170	22.31(1.00)	3.85(0.172)	1.51(0.068)	27.67
0.0350	22.05(1.00)	4.19(0.190)	3.43(0.155)	29.67
0.0700	50.02(1.00)	5.15(0.103)	4.86(0.097)	60.03
0.1400	63.49(1.00)	11.22(0.177)	6.52(0.103)	81.23
0.2800	54.91(1.00)	23.41(0.426)	6.61(0.120)	84.93
0.5600	57.92(1.00)	31.71(0.547)	4.78(0.082)	94.41
1.120	33.98(1.00)	23.78(0.700)	2.15(0.063)	59.91
2.240	9.61(1.00)	39.64(4.124)	6.18(0.642)	55.43
4.480	0.00	17.96	20.42	38.38

TABLE VIII

PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $\text{Cu}(\text{AcAc})_2$ CONCENTRATION OF THE
REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	6.55(1.00)	0.51(0.078)	0.87(0.134)	7.93
0.0085	6.86(1.00)	0.62(0.090)	0.86(0.125)	8.34
0.0170	51.48(1.00)	7.18(0.139)	4.63(0.090)	63.29
0.0350	40.76(1.00)	3.10(0.076)	5.58(0.137)	49.44
0.0700	71.47(1.00)	7.93(0.111)	6.19(0.087)	85.59
0.1400	78.08(1.00)	12.39(0.158)	5.92(0.076)	96.39
0.2800	69.24(1.00)	19.57(0.283)	6.44(0.093)	95.25
0.5600	55.43(1.00)	34.44(0.621)	5.00(0.090)	94.87
1.120	48.65(1.00)	20.93(0.430)	7.52(0.154)	77.10
2.240	42.04(1.00)	6.87(0.163)	4.76(0.113)	53.67
4.480	22.48(1.00)	2.82(0.125)	6.37(0.284)	31.67

TABLE IX

PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF (i-Pr-o)₃P-CuCl CONCENTRATION IN
THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE

Catalyst (mmole)	I	IX	II	Total Product
0.0042	18.70(1.00)	1.61(0.086)	1.89(0.102)	22.20
0.0085	30.55(1.00)	4.71(0.154)	2.49(0.081)	37.75
0.0170	30.20(1.00)	4.71(0.156)	2.06(0.067)	36.97
0.0350	42.90(1.00)	5.08(0.118)	3.26(0.080)	51.24
0.0700	48.82(1.00)	5.33(0.124)	3.43(0.072)	57.58
0.1400	61.52(1.00)	11.77(0.191)	4.72(0.077)	78.01
0.2800	58.26(1.00)	7.18(0.123)	4.12(0.082)	69.56
0.5600	66.50(1.00)	8.92(0.134)	5.40(0.084)	80.82
1.120	51.31(1.00)	14.37(0.280)	3.86(0.076)	69.54
2.240	16.90(1.00)	28.74(1.70)	1.80(0.115)	47.44
4.480	6.95(1.00)	26.63(3.83)	1.29(0.181)	34.87

TABLE X
PRODUCT DISTRIBUTION AND YIELDS IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH
1-METHYLCYCLOHEXENE USING $(\text{CH}_3\text{O})_3\text{P}-\text{CuCl}$ AS CATALYST AT 110°C

Catalyst (mmole)	III	IV	V	VI	IX	Total Insertion	Total Product
0.0042	21.53(1.00)	1.51(0.070)	7.78(0.361)	19.54(0.904)	4.03(0.187)	28.81	54.37
0.0085	23.07(1.00)	1.68(0.073)	8.72(0.378)	20.12(0.874)	3.84(0.166)	30.56	57.47
0.0170	22.34(1.00)	1.63(0.073)	8.45(0.378)	19.59(0.877)	2.48(0.111)	29.67	54.49
0.0350	21.80(1.00)	1.68(0.077)	8.05(0.369)	18.91(0.868)	3.56(0.163)	28.64	54.00
0.0700	23.21(1.00)	1.80(0.077)	8.38(0.361)	20.39(0.878)	3.69(0.159)	30.57	57.47
0.1400	20.39(1.00)	1.45(0.071)	7.11(0.349)	16.90(0.830)	4.78(0.234)	25.46	50.63
0.2800	20.12(1.00)	1.54(0.077)	7.98(0.396)	19.45(0.965)	3.84(0.191)	28.97	52.93
0.5600	19.38(1.00)	1.49(0.077)	7.44(0.384)	18.71(0.966)	5.08(0.262)	27.64	52.10
1.120	18.51(1.00)	0.01(0.055)	7.63(0.358)	14.89(0.805)	7.77(0.420)	22.53	48.81
2.240	8.72(1.00)	0.40(0.046)	3.76(0.431)	9.05(1.04)	22.67(2.60)	13.20	44.59
4.480	6.77(1.00)	0.00	2.07(0.307)	4.81(0.715)	19.32(2.87)	6.88	32.97

TABLE XI

PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ CONCENTRATION IN THE
REACTION DIMETHYL DIAZOMALONATE WITH 1-METHYLCYCLOHEXENE AT 85°C

Catalyst (mmole)	III	IV	V	VI	IX	Total Insertion	Total Product
0.0042	8.65(1.00)	0.62(0.072)	1.46(0.169)	1.05(0.122)	2.70(0.312)	3.13	14.48
0.0085	7.24(1.00)	0.63(0.087)	0.79(0.109)	1.26(0.174)	2.32(0.320)	2.68	12.24
0.0170	4.39(1.00)	1.01(0.230)	1.47(0.334)	1.01(0.230)	4.76(0.230)	3.49	12.64
0.0350	9.99(1.00)	0.58(0.057)	2.89(0.290)	6.98(0.693)	3.20(0.320)	10.45	23.64
0.0700	6.20(1.00)	0.17(0.027)	1.11(0.179)	2.85(0.458)	1.24(0.200)	4.13	11.57
0.1400	9.59(1.00)	0.00	2.52(0.262)	9.86(1.03)	1.55(0.162)	12.38	23.52
0.2800	18.04(1.00)	1.03(0.057)	5.16(0.286)	19.72(1.09)	8.56(0.474)	25.91	52.51
0.5600	9.32(1.00)	0.49(0.052)	2.11(0.224)	9.46(1.01)	2.29(0.246)	12.06	23.67
1.120	10.66(1.00)	1.56(0.146)	2.56(0.240)	14.76(1.38)	15.24(1.43)	18.88	44.78
2.240	6.71(1.00)	0.00	2.58(0.385)	8.25(1.23)	22.17(3.30)	11.10	39.98
4.480	4.40(1.00)	0.00	1.53(0.348)	3.26(0.740)	25.52(5.80)	4.79	34.71

TABLE XII

PRODUCT DISTRIBUTION AND YIELDS IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH 1-METHYLCYCLOHEXENE
USING $(\text{CH}_3\text{O})_3\text{P-CuCl}$ AS CATALYST IN REFLUXING HEXAFLUOROBENZENE AT 83°C (90 mole percent HFB)

Catalyst (mmole)	III	IV	V	VI	IX	Total Insertion	Total Product
0.0042	12.74(1.00)	0.21(0.017)	0.94(0.074)	6.14(0.480)	6.09(0.478)	7.29	26.12
0.0085	13.08(1.00)	0.23(0.017)	0.98(0.075)	6.77(0.518)	6.40(0.489)	7.98	27.46
0.0170	11.74(1.00)	0.34(0.029)	1.01(0.086)	3.35(0.286)	3.10(0.264)	4.70	19.54
0.0350	24.62(1.00)	1.08(0.044)	1.62(0.066)	27.84(1.13)	7.99(0.324)	30.54	63.15
0.0700	11.34(1.00)	0.45(0.039)	1.56(0.137)	6.20(0.546)	3.91(0.345)	8.21	23.46
0.1400	10.73(1.00)	0.91(0.084)	2.45(0.228)	5.59(0.521)	4.39(0.409)	8.95	24.07
0.2800	23.34(1.00)	0.75(0.032)	1.50(0.064)	26.16(1.12)	13.87(0.594)	28.41	65.62
0.5600	18.58(1.00)	0.84(0.043)	1.56(0.084)	21.53(1.16)	24.28(1.31)	23.93	66.79
1.120	13.41(1.00)	0.53(0.039)	0.83(0.061)	14.49(1.08)	39.14(2.92)	15.84	68.39
2.240	10.06(1.00)	0.56(0.055)	1.79(0.178)	12.27(1.22)	44.47(4.42)	14.62	69.15
4.480	9.19(1.00)	0.59(0.064)	2.23(0.243)	5.88(0.640)	38.65(4.21)	8.70	56.54

TABLE XIII

EFFECT OF ANION UPON PRODUCT DISTRIBUTION AND YIELDS IN THE REACTION
OF CYCLOHEXENE WITH DIMETHYL DIAZOMALONATE

0.14 mmole (CH ₃ O) ₃ P-CuX	I	IX	II
X= BF ₄ [*]	59.55(1.00)	7.25(0.122)	8.09(0.136)
I	74.23(1.00)	12.88(0.174)	7.42(0.101)
Br	68.64(1.00)	15.11(0.220)	6.68(0.097)
Cl	63.92(1.00)	13.25(0.207)	4.69(0.074)
SCN	28.31(1.00)	1.31(0.046)	1.82(0.064)
CN	41.53(1.00)	0.81(0.020)	0.94(0.023)

*Concentration less than 0.14 mmole due to decomposition during transfer.

TABLE XIV

EFFECT OF COMMON ION ON THE REACTION OF CYCLOHEXENE WITH
DIMETHYL DIAZOMALONATE

Catalyst	Salt	I	IX	II
(CH ₃ O) ₃ P-CuI	none	74.23(1.00)	12.88(0.174)	7.42(0.101)
(CH ₃ O) ₃ P-CuI	(CH ₃) ₄ NI	3.33(1.00)	0.00	7.08(2.12)
(CH ₃ O) ₃ P-CuI	(CH ₃) ₄ NBF ₄	63.66(1.00)	11.36(0.178)	5.00(0.078)
(CH ₃ O) ₃ P-CuCl	none	63.92(1.00)	13.25(0.207)	4.69(0.074)
(CH ₃ O) ₃ P-CuCl	(CH ₃) ₄ NCl	8.58(1.00)	1.57(0.183)	0.00
(CH ₃ O) ₃ P-CuCl	(CH ₃) ₄ NBF ₄	49.33(1.00)	5.26(0.107)	4.08(0.083)

TABLE XV

SOLVENT EFFECTS IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH
CYCLOHEXENE USING $(\text{CH}_3\text{O})_3\text{P}-\text{CuCl}$ (0.14 mmole) AS CATALYST

Solvent (90%)	I	IX	II
Cyclohexene	63.92(1.00)	13.25(0.207)	4.69(0.074)
Cyclohexene	31.23(1.00)	52.52(1.681)	3.90(0.125)
Benzene	57.91(1.00)	39.64(0.684)	3.34(0.058)
Hexafluorobenzene	81.00(1.00)	15.86(0.196)	4.24(0.052)
Carbon tetrachloride	28.31(1.00)	5.71(0.202)	31.66(1.13)
Dimethoxyethane	0.00	0.00	0.00

TABLE XVI

EFFECT OF ADDITIVES UPON YIELDS AND PRODUCT DISTRIBUTION IN THE
REACTION OF CYCLOHEXENE WITH DIMETHYL DIAZOMALONATE USING
 $(\text{CH}_3\text{O})_3\text{P}-\text{CuCl}$ (0.14 mmole) AS CATALYST

Additive (mmole)	I	IX	II
None	63.92(1.00)	13.25(0.207)	4.69(0.074)
CuCl	33.46(1.00)	33.44(1.00)	2.29(0.071)
$(\text{CH}_3\text{O})_3\text{P}$	46.07(1.00)	21.18(0.460)	3.75(0.082)
$(\text{CH}_3\text{O})_3\text{PO}$	68.13(1.00)	16.23(0.238)	5.92(0.087)
$(\text{CH}_3\text{O})_2\text{CH}_3\text{PO}$	60.58(1.00)	19.20(0.316)	5.08(0.084)
$[(\text{CH}_3)_2\text{N}]_3\text{P}$	49.94(1.00)	24.28(0.486)	4.61(0.092)
$[(\text{CH}_3)_2\text{N}]_3\text{PO}$	45.82(1.00)	17.34(0.378)	3.72(0.081)
CuCl_2	55.00(1.00)	17.96(0.326)	5.34(0.097)
$(\text{CH}_3\text{O})_2\text{HPO}$	59.54(1.00)	25.14(0.422)	4.48(0.077)

TABLE XVII

EFFECT OF PEROXIDE UPON THE REACTION OF CYCLOHEXENE WITH DIMETHYL DIAZOMALONATE

Catalyst (0.14 mmole)	Conditions	I	IX	II
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	A	74.23(1.00)	12.88(0.174)	7.42(0.101)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	B	19.38(1.00)	2.02(0.104)	1.79(0.092)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	C	72.02(1.00)	11.35(0.157)	5.28(0.074)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	D	67.78(1.00)	12.09(0.178)	6.27(0.093)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	A	68.64(1.00)	15.11(0.220)	6.68(0.097)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	B	21.96(1.00)	1.88(0.086)	2.08(0.094)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	C	69.76(1.00)	14.24(0.204)	5.54(0.080)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	D	67.35(1.00)	11.77(0.175)	5.46(0.081)
None	C	9.44(1.00)	1.83(0.194)	0.00

A. Untreated, commercial cyclohexene.

B. Commercial cyclohexene filtered through alumina.

C. Condition B, then benzoyl peroxide (0.07 mmole) added.

D. Condition B, then Vazo (0.07 mmole) added.

TABLE XVIII

EFFECT OF BENZOYL PEROXIDE^a ON THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE
AT VARIOUS CONCENTRATIONS OF $(\text{CH}_3\text{O})_3\text{PCuX}$

Catalyst	Conc. (mmole)	I	IX	II
X=I	0.0700	73.79(1.00)	12.39(0.168)	5.32(0.072)
I	0.1400	75.95(1.00)	15.98(0.210)	5.88(0.077)
I	0.2800	68.90(1.00)	27.01(0.392)	5.06(0.074)
Br	0.0700	71.73(1.00)	13.13(0.183)	5.49(0.077)
Br	0.1400	71.56(1.00)	23.91(0.334)	5.72(0.080)
Br	0.2800	70.96(1.00)	19.45(0.274)	5.86(0.081)
Cl	0.0700	79.36(1.00)	17.96(0.226)	6.01(0.076)
Cl	0.1400	78.51(1.00)	13.05(0.172)	6.24(0.079)
Cl	0.2800	50.52(1.00)	37.41(0.740)	3.36(0.067)

^a Olefins were filtered through alumina and benzoyl peroxide added to give a 1 : 1 mixture of benzoyl radicals and catalyst.

TABLE XIX

EFFECT OF PREOXIDIZED CATALYST UPON THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE^a

Catalyst	Method of Oxidation	I	IX	II
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	A	76.36(1.00)	18.58(0.243)	6.00(0.079)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	B	75.68(1.00)	13.00(0.173)	5.64(0.075)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	B (Extracted)	69.67(1.00)	9.91(0.142)	4.72(0.068)
CuI	Benzoyl Peroxide	67.35(1.00)	4.04(0.059)	4.04(0.060)
CuI	Benzoyl Peroxide ^c	68.49(1.00)	9.36(0.137)	6.91(0.101)
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	B ^b	79.96(1.00)	10.73(0.134)	6.30(0.079)

^aAll samples of cyclohexene were treated with alumina immediately before use.^bAddition of dimethyl diazomalonate carried out in the presence of 0.1 g of p-dinitrobenzene.^cOxidized product recrystallized from tetrahydrofuran.

TABLE XX

EFFECT OF MISCELLANEOUS CATALYSTS ON THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE^a

Catalyst			
$[(CH_3O)_3P]_2CuI$	65.81(1.00)	19.20(0.292)	6.58(0.100)
$[(CH_3O)_3P]_3CuI$	63.49(1.00)	11.22(0.177)	6.52(0.103)
$(PhO)_3P-CuBr$	72.93(1.00)	13.25(0.182)	7.43(0.102)
$AgBF_4$	19.73(1.00)	5.93(0.301)	3.94(0.199)
$(QH)_2CuBr_4^c$	7.25(1.00)	8.38(1.16)	0.00
$(QH)_2CuCl_4^c$	11.50(1.00)	25.51(2.22)	1.65(0.069)
$(CH_3O)_3P-ZnI_2$	3.77(1.00)	2.72(0.723)	0.00
$C_9H_8O_4Cu \cdot H_2O^b$	75.08(1.00)	3.86(0.051)	7.32(0.096)

^aIn all cases, 0.14 mmole of catalyst was used.^bThis material was generously supplied by Laurence Campbell.^cQH represents quinuclidium. These compounds were generously supplied by Richard Dickenson.

Competition Studies

Equimolar amounts of cyclohexene and 1-methylcyclohexene were mixed and treated with dimethyl diazomalonate in the usual way using $(\text{CH}_3\text{O})_3\text{P-CuI}$ as catalyst. The resulting product distribution is shown in Table XXI.

TABLE XXI

PRODUCT DISTRIBUTION FROM THE REACTION OF DIMETHYL DIAZOMALONATE WITH EQUIMOLAR AMOUNTS OF CYCLOHEXENE AND 1-METHYLCYCLOHEXENE

Product	Relative Yield
I	1.000
II	0.000
III	0.204
IV	0.018
V	0.072
VI	0.118

The addition of dimethyl diazomalonate to an equimolar mixture of cis- and trans-2-heptene was carried out in the usual way using $(\text{CH}_3\text{O})_3\text{P-CuI}$ as catalyst. G.c. analysis of the reaction mixture showed 5.20 parts of the cis-cyclopropane to 1.00 part of the trans adduct.

Interrupted Reactions

A solution of 0.14 mmole of $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$ was dissolved in 25 ml of refluxing cyclohexene and a solution of 0.316 g (2.0 mmole) of dimethyl diazomalonate in 2.5 ml of cyclohexene (10% of a normal run) was added in the usual way. The reaction was repeated at 30% of a normal run. The yields and product distribution from these reactions are shown in the following table.

TABLE XXII

EFFECT OF AMOUNT OF AVAILABLE DIMETHYL DIAZOMALONATE ON ITS REACTION WITH CYCLOHEXENE UNDER OPTIMUM CONDITIONS USING $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$

Conditions	I	IX	II
10% Usual Reaction	0.15(1.00)	0.00	0.270(0.515)
Expected Yields for 10%*	7.35(1.00)	1.15(0.157)	0.598(0.081)
30% Usual Reaction	12.10(1.00)	2.10(0.174)	1.36 (0.113)
Expected Yields for 30%*	22.05(1.00)	3.45(0.157)	1.79 (0.081)
Expected Yields for 20%*	14.70(1.00)	2.30(0.157)	1.20 (0.081)

* Expected yields based on optimized yield using $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$

STEREOCHEMICAL STUDIES

Reaction of Ethyl Diazoacetate with Cyclohexene

Cyclohexene was treated with ethyl diazoacetate (0.02 mole) under conditions described earlier for dimethyl diazomalonate. The mono, bis, and tris trimethylphosphite complexes of copper(I) iodide were used as catalysts. The resulting yields and product distributions are shown in the following table and are relative to an internal standard.

TABLE XXIII

PRODUCT DISTRIBUTION IN THE REACTION OF CYCLOHEXENE WITH ETHYL DIAZOACETATE USING $[(CH_3O)_3P]_n \cdot CuI$ AS CATALYST

Catalyst (mmole)	n	Norcarane			Dimer		
		exo	endo	ratio	cis	trans	ratio
0.140	1	7.80	0.65	12.0	0.088	0.123	0.715
5.00	1	2.91	1.16	2.51	0.218	0.710	0.307
0.140	2	7.87	0.684	11.5	0.100	0.150	0.667
5.00	2	0.965	0.946	1.02	0.077	0.254	0.304
0.140	3	8.05	0.533	15.1	0.067	0.111	0.608
5.00	3	0.333	0.832	0.40	0.00	0.00	

Stereospecificity Study

Dimethyl diazomalonate was added to cis- and trans-2-heptene under a variety of conditions. In all cases, a small portion of the reaction mixture was treated with bromine-carbon tetrachloride solution

in order to distinguish insertion products from cyclopropyl products. The cis olefin was 96% pure and the trans isomer 99% pure. The results of this study are shown in the table below in terms of per cent yield based on consumed diazo compound.

TABLE XXIV
PRODUCTS AND YIELDS FROM THE REACTION OF DIMETHYL
DIAZOMALONATE WITH 2-HEPTENES

(CH ₃ O) ₃ P·CuX (0.14 mmole)	Isomer	Temp. °C	Cyclopropyl		Insertion	Dimer
			Cis	Trans		
X=I	<u>Cis</u>	98	95.6	Trace	0.52	3.36
I	<u>Cis</u>	85	92.1	Trace	3.30	4.64
Br	<u>Cis</u>	85	87.6	Trace	7.08	5.32
Cl	<u>Cis</u>	85	81.3	Trace	12.8	6.00
I	<u>Trans</u>	98	0.00	76.0	6.60	17.4
I	<u>Trans</u>	85	0.00	69.8	18.6	11.6
Br	<u>Trans</u>	85	0.00	72.5	18.4	9.20
Cl	<u>Trans</u>	85	0.00	41.7	35.2	23.1

INVESTIGATION OF POSSIBLE INTERMEDIATES

Preparation of Dimethyl Mesoxalate Triethylphosphorazine

Dimethyl mesoxalate triethylphosphorazine was prepared by the method of Poshkus and Herweh.¹⁶ A solution of 83.0 g (0.5 mole) of triethylphosphite in 200 ml of pentane was stirred at room temperature while 79.0 g (0.5 mole) of dimethyl diazomalonate in 200 ml of pentane was added over 2 hours. During the addition, the temperature rose to 34°C and a pentane oil formed. The yellow oil was removed and washed five times with pentane. An attempt to distill a portion of the material ended in its rapid decomposition at a pot temperature of 35-40°C. The pentane was removed under vacuum without heat and the phosphorazine used without further purification. The n. m. r. spectrum (CCl_4) showed a pentuplet centered at τ 5.75 (6H, methylene), a singlet at τ 6.22 (6H, COOMe), a triplet centered at τ 8.62 (9H, Me), and a small amount of impurity (mostly pentane). The compound was assigned the structure dimethyl mesoxalate triethylphosphorazine.

Preparation of Dimethoxycarbonylmethylenetriphenylphosphorane

Dimethoxycarbonylmethylenetriphenylphosphorane was prepared by a modified procedure based on the method of Horner and Oediger.¹⁷ A solution of 131 g (0.5 mole) of triphenylphosphine in 1400 ml of dry benzene was cooled to 10°C. With stirring, a solution of 25.8 ml (0.5 mole) of bromine in 50 ml of carbon tetrachloride was added over 2 hours. When the addition was complete, a solution of 121.4 g (1.2 mole) of triethylamine and 66.0 g (0.5 mole) of dimethyl malonate in 400 ml of benzene was added all at once. The solution was heated at reflux for 10 minutes then allowed to cool. The solid which formed

(triethylamine hydrobromide) was removed by filtration and the solvent removed by distillation to leave a red oil. The oil solidified upon the addition of pentane. The solid was filtered, dissolved in cyclohexane, treated with activated charcoal, then allowed to crystallize. After two recrystallizations, 156 g (80%) of light yellow crystals melting at 142-143°C were collected. The infrared spectrum (KBr) showed bands at 1195 cm^{-1} (s, P=C) and 1640 cm^{-1} (m, C=O). The spectrum was almost identical to that reported for diethoxycarbonylmethylenetriphenylphosphorane.¹⁸ The n. m. r. spectrum (COCl_3) showed a doublet centered at τ 6.20 (6H, COOEt) and a multiplet centered at τ 2.50 (15H, aromatic).

Decomposition of Dimethyl Mesoxalate Triethylphosphorazine

A 5.54 g (0.02 mole) sample of dimethyl mesoxalate triethylphosphorazine was decomposed to cyclohexene as previously described for dimethyl diazomalonate. Trimethylphosphite copper(I) chloride (0.14 mmole) was used as catalyst. During the addition, a dark insoluble oil formed. Both the oil and the cyclohexene layer were analyzed by g.c. None of the normal carbene addition products were present in either phase of the reaction mixture.

The procedure was repeated using copper(I) chloride as catalyst. Again, no recognizable products were formed.

Decomposition of Dimethoxycarbonylmethylenetriphenylphosphorane

The decomposition was carried out as described above for dimethyl mesoxalate triethylphosphorazine using both complexed and uncomplexed copper(I) chloride. G.c. analysis of the reaction mixture showed the absence of all the products typical of the carbene additions.

BASE CATALYZED REACTIONS

Reaction of 7,7-Dimethoxycarbonylnorcarane with Potassium t-Butoxide

A solution of 21.2 g (0.10 mole) of 7,7-dimethoxycarbonylnorcarane and 1.12 g (0.1 mole) of potassium t-butoxide in 400 ml of dry t-butyl alcohol was warmed to about 40°C under nitrogen. G.c. analysis of the reaction mixture after 12 hours showed 20% starting material and 80% of a new compound. Longer reaction time and the addition of more base failed to increase the amount of conversion. The solution was diluted with 200 ml of water and neutralized with dilute hydrochloric acid. After removal of the alcohol, the organic layer was removed and the aqueous layer extracted three times with 50 ml of ether. The combined organic layers were washed with 25 ml of water and 25 ml of saturated sodium chloride solution and dried over anhydrous sodium sulfate. After removal of the ether, the oil was distilled to give only one component, boiling at 76-78°C/0.05 mm. The unreacted ester sublimed directly into the cold trap during the distillation. A sample of the oil was crystallized from methanol to furnish crystals, m.p. 39.5-40.5°C. The n. m. r. spectrum (CCl_4) showed a singlet at τ 6.27 (3H, COOMe), and unresolved absorption between τ 7.84 and τ 9.10 (19H) including a sharp singlet at τ 8.60 (approximately 9H, COOtBu). Analysis calculated for $\text{C}_{14}\text{H}_{22}\text{O}_4$: C, 66.14; H, 8.66. Found: C, 66.30; H, 8.65. On the basis of the above data and the known chemistry of the system, the compound was tentatively assigned the structure 7-exo-t-butoxycarbonyl-7-endo-methoxycarbonylnorcarane. This was shown conclusively by the following structure proof.

The t-butyl ester was cleaved by the method used by Fonken and

Johnson¹⁹ to prepare substituted malonic esters. A 2.54 g (0.01 mole) sample of the mixed ester and 5 mg of anhydrous p-toluenesulfonic acid²¹ in dry toluene (25 ml) were heated at reflux. A gas was evolved which rapidly decolorized a carbon tetrachloride solution of bromine (isobutylene). When no more gas was given off, the solution was concentrated to 5 ml and cooled. The crystals which formed were collected and dried. A total of 1.90 g of white solid melting at 112-114°C was collected. The melting point was not raised by recrystallization from methanol. The n. m. r. spectrum showed a singlet at τ -1.53 (1H, COOH), a singlet at τ 6.24 (3H, COOMe), and broad overlapping multiplets centered at τ 8.09 and τ 8.80 (total 10H, ring protons). Analysis calculated for $C_{10}H_{14}O_4$: C, 60.61; H, 7.07. Found: C, 60.75; H, 7.17. The compound was tentatively assigned the structure 7-endo-methoxycarbonyl-7-exo-carboxynorcarane. The yield based on that structure was 97%.

A 2.0 g sample of 7-endo-methoxycarbonyl-7-exo-carboxynorcar-3-ene (prepared by known methods²¹ and generously supplied by Brad McGiboney) was taken up in 200 ml of ethanol, 1.00 g of 5% Rh on alumina added, and the material hydrogenated in a Joshel atmospheric hydrogenation apparatus until one mole of hydrogen had been consumed. The catalyst was removed by filtering, and the solution concentrated to 10 ml and the acid allowed to crystallize. The solid was collected, dried, and shown by m.p., n. m. r., and infrared to be identical to the acid formed by cleavage of the t-butyl ester above.

Reaction of 7,7-Dimethoxycarbonylnorcarane with Potassium Cyanide

A solution of 5.3 g (0.025 mole) of 7,7-dimethoxycarbonylnorcarane and 3.25 g (0.05 mole) of potassium cyanide in 75 ml of dry dimethylform-

amide was heated at reflux for 12 hours, by which time a solid had formed. G.c. analysis of the supernatant liquid showed none of the starting diester. The solvent was removed under vacuum, the solid suspended in ether, filtered and washed several times with ether. The combined ether solutions were washed with water, saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the ether gave 1.5 g (34%) of an oil which was identified as exo- and endo-7-methoxycarbonylnorcarane (9:1) by comparison of their g.c. retention times to those of authentic samples.

The solid portion of the reaction mixture was dissolved in 25 ml of water and neutralized (hood) with concentrated hydrochloric acid. The aqueous solution was extracted three times with chloroform. The chloroform solutions were combined and concentrated to leave a white solid, which after three recrystallizations from chloroform, melted at 186-188°C. The compound was identified as 7,7-norcaranedicarboxylate by m.p., mixed m.p. and infrared comparison to authentic material. the yield was 65%. The reported m.p. of the diacid is 186-188°C.²¹

General Procedure for Attempted Base Catalyzed Ring Openings

Solutions of 0.01 mole each of 7,7-dimethoxycarbonylnorcarane, base, and nucleophile in various solvents were heated at reflux under nitrogen. Periodically, samples were removed from the reaction mixture, dissolved in water and neutralized with dilute hydrochloric acid. The solutions were extracted with ether, the ether solutions concentrated and the samples analyzed by g.c. All attempted reactions were heated at reflux for a minimum of 48 hours. The results of this study are shown in Table XXV.

TABLE XXV
ATTEMPTED BASE CATALYZED RING OPENING REACTIONS

Solvent	Temp. °C	Base	Nucleophile	Result
Benzene	80	NaH	$\text{H}_2\text{C}(\text{COOMe})_2$	no reaction ^d
Benzene	80	NaH	$\text{Ph}-\text{C}=\text{CH}$	no reaction
MeOH	64	NaOMe	$\text{H}_2\text{C}(\text{COOMe})_2$	no reaction
MeOH	64		KCN	no reaction
MeOH	64	NaOMe	$\text{H}_2\text{C}(\text{CN})_2$	no reaction
$\text{H}_2\text{C}(\text{COOMe})_2$	180	NaH	$\text{H}_2\text{C}(\text{COOMe})_2$	no reaction
DMSO^a	198	NaH	$\text{H}_2\text{C}(\text{COOMe})_2$	no reaction
DMSO	198	NaH	$\text{H}_2\text{C}(\text{CN})_2$	no reaction
DMSO	198	NaH	$\text{Ph}-\text{C}=\text{CH}$	no reaction
DMF^b	153	NaH	$\text{H}_2\text{C}(\text{COOMe})_2$	no reaction
DMF	153	NaH	$\text{H}_2\text{C}(\text{CN})_2$	no reaction
DMF	153	NaH	$\text{Ph}-\text{C}=\text{CH}$	no reaction
DMF	153	NaH	MeCOOtBu	no reaction
HMPA^c	232	NaH	$\text{H}_2\text{C}(\text{COOMe})_2$	no reaction
HMPA	232	NaH	$\text{Ph}-\text{C}=\text{CH}$	no reaction
HMPA	232	ThOEt	$\text{Ph}-\text{C}=\text{CH}$	no reaction

^aDimethyl sulfoxide

^bDimethylformamide

^cHexamethylphosphoramide

^dIn all cases, lack of any reaction was confirmed by recovery of 90% or more of the 7,7-dimethoxycarbonylnorcarane.

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CHAPTER VI

RESULTS AND DISCUSSION

RESULTS AND DISCUSSION

Several portions of this work have been discussed in detail in references 1-9 and in chapters 1 and 2 of this thesis. The subjects covered thoroughly in the above papers will not be discussed here.

Phosphites

During the course of this study, a number of phosphite copper(I) complexes of the type $(RO)_3P_n \cdot CuX$ (R =alkyl or aryl, $n=1, 2$, or 3 ; and $X=Cl^-$, Br^- , I^- , CN^- , SCN^- , and BF_4^-) were prepared and their efficacy in carbenoid generation tested. Most often, these complexes were prepared by the method introduced by Arbuzov^{10,11} and more recently used by Moser¹² and Nishizawa.¹³ In this procedure, the phosphite was mixed with the appropriate mole ratio of copper(I) salt in benzene, followed by evaporation to dryness and recrystallization of the complex from chloroform. A modification of this process, made during this work, greatly simplified the synthesis.⁵ Thus, addition of an alcohol to the concentrated benzene solution (see above) causes instant precipitation of the complex. Material obtained in this way is pure and need not be recrystallized. The alcohol to be used should correspond to the phosphite portion of the complex; and aliphatic alcohols should not be used with aryl phosphite complexes, since rapid ester exchange occurred under these conditions. The use of chloroform as a recrystallization solvent should be avoided. The complexes dissolved readily in this solvent, but an insoluble material formed after a few minutes. Halogenated hydrocarbons are known to react with phosphites.¹⁴ This reaction probably destroyed the complexes, giving the free copper salt.

Nishizawa¹³ reported his inability to prepare a tris(phosphite) copper(I) halide complex. The author did not specify the exact phosphite used in this attempt, however, most of his work centered around tri-iso-propyl- and triphenylphosphite. The present work has shown that tris(trimethylphosphite) copper(I) iodide is easily prepared by the modified Arbuzov procedure. Nishizawa's results might be explained in terms of steric considerations. However, triphenylphosphite formed both mono and bis complexes with copper(I) chloride and bromide, while only the bis complex was obtained from the iodide salt irrespective of the mole ratio or reactants.^{10,11}

In a few cases, phosphite copper(I) complexes were prepared by the method of Beriger.¹⁵ This procedure involved the addition of phosphorous trihalide to a mixture of copper salt and an alcohol in toluene and led to impure material. Beriger's method is a potentially attractive route to complexes derived from phosphites which are not readily available.

This author has shown that trialkylphosphite copper(I) halide complexes can also be prepared by the action of a phosphite upon copper(II) salts. This procedure gives impure products and is inferior to our modification of the Arbuzov procedure. While this work was in progress, Carty and coworkers¹⁶ introduced a similar reductive procedure for the synthesis of trialkylphosphine copper(I) complexes.

The properties of trimethylphosphite copper(I) chlorides obtained from the three different schemes discussed are of interest. The infrared spectra of the complexes from all three preparations are identical, although the P^{31} n. m. r. patterns and their melting points are distinctly different. Whether this is a result of impurities, poly-

morphism, aggragation, or some other factor is not known.

Most of the trialkylphosphite copper(I) complexes used in this work were known to the literature. It should be noted, however, that almost all melting points reported in the older literature^{10,11} for these complexes were incorrect, several by as much as 40°C. Some of these discrepancies were noted earlier by Nishizawa.¹³ Table I compares the melting points found during this work to those obtained by Arbuzov and Nishizawa. Low melting points appear to be due to impure

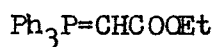
TABLE I
MELTING POINTS OF TRIALKYLPHOSPHITE COPPER(I) HALIDES

Complex	Arbuzov	Nishizawa	This work
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$	190-2		229-30
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuBr}$	180-2		226-28
$(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	175-7		193-5
$(\text{iso-C}_3\text{H}_7\text{O})_3\text{P}\cdot\text{CuCl}$	112-14	117	117-118
$(\text{iso-C}_3\text{H}_7\text{O})_3\text{P}\cdot\text{CuI}$	184-5	199-200	199.5-200

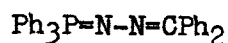
copper salts since freshly prepared copper(I) chloride routinely gave the higher melting complexes.

Possible Phosphorus Intermediates

The possible intermediacy of certain phosphorus compounds in the reactions of diazomalonate was studied. Compounds (1)¹⁷ and (2)¹⁸ are known to furnish products formally derivable from typical carbene reaction. The malonate analogues of (1) and (2) resulted in tar



(1)



(2)

formation and no recognizable products when decomposed in cyclohexene.

Copper Catalysis

The nature of the active catalyst species in copper and copper salt diazo decompositions has been the subject of much discussion.¹⁹ Two groups have observed the reduction of copper(II) chloride to copper(I) chloride by diazomethane and suggested the lower oxidation state was the actual catalyst.^{20,21} D'yakonov²² observed the formation of metallic copper from copper(II) sulfate during the decomposition of ethyl diazoacetate. The results of this study, however, clearly indicated that copper(II) was either the actual catalyst or, at least, a far more active catalyst than either elemental copper or copper(I).²

The oxidation of copper(0)²³ and copper(I)²⁴ by organic free radicals is well known and invariably peroxide impurities are present in olefins unless very special precautions are employed. This author has observed the oxidation of copper(I) iodide (both complexed and uncomplexed) by excess benzoyl peroxide. In the absence of an added radical source, peroxide impurities in the olefin served to oxidize the copper(I) complex. This was conclusively demonstrated by the failure of ultra pure olefins to react in a normal manner with diazo-malonates and copper(I) complexes.

In the reaction of dimethyl diazomalonate with cyclohexene employing trimethylphosphite copper(I) halide catalyst, it was never possible to account for all the available diazo compound at the end of a reaction. Analysis of the reaction mixture after 10% of the

diazomalonate has been added showed no recognizable products. After the first 10%, the reaction proceeded in a normal manner and after 30% reaction the product distribution was similar to those normally seen after allowing the reaction to go to completion. Thus, an initial pre-reaction can be postulated involving oxidation of copper(I) to the active species after which the reaction proceeds to the usual product distribution.

The oxidation step was also indicated by the effects of several additives. The addition of trivalent phosphorus compounds reduced the efficacy of the copper phosphite catalyst but pentavalent phosphorus compounds did not. As trivalent phosphorus compounds are known to react with peroxides,²⁵ this would reduce the peroxide available to oxidize copper(I) and give a poorer reaction. Alternatively this effect can be reasonably attributed to phosphinazene formation.

The oxidation of copper(I) iodide by excess benzoyl peroxide has been shown to liberate iodine. This was not the case with limited levels of peroxides or in the presence of phosphites. The oxidized catalyst must have contained a copper to halogen bond since a definite anion effect and a common ion effect were observed.⁴ Therefore, a copper(II)-alkoxyhalide (or anion) would appear to be the active species (Eq. 1). Copper(II) might have been the active catalyst in



EQUATION 1

almost all studies reported to date. Considering the very low catalyst concentration necessary for optimum results, most olefins probably contained sufficient peroxides to have generated the copper(II) ion. In the case of complex ions and copper(I) salts the presence of small amounts of copper(II) impurities would be expected except with copper iodide.

Moser¹² employed very pure olefins, but the actual catalyst used in his work was not established in view of the present study. Without mentioning optimum catalyst concentrations, Moser employed almost twenty times the optimum concentration of the copper(I) phosphite complexes employed in this study. Copper(I) may have served as a less active catalyst. On the other hand, low concentrations of copper(II) could have been generated by traces of air present, diazo compound, by radicals from phosphenazene decompositions, or impure complexes (Moser did not furnish physical constants for his copper(I) phosphite complexes and we found that the melting points are depressed by copper(II) impurities but the melting point ranges remained narrow).

Structure Assignments

The copper, copper salt, and copper complex catalyzed decompositions of diazo compounds normally do not yield C-H insertion products.¹⁹ As reported earlier,⁴ this work has shown C-H insertion to be a major side reaction when diazomalonates are employed.

The insertion reaction of carbenes in general usually occur at the most acidic C-H bond, which, in the case of cyclohexene, is the allylic position. The decomposition of dimethyl diazomalonate in cyclohexene was shown by g.c. analysis to give three products: I, II

and IX. Compounds I and IX were on hand in this laboratory and II was prepared by an independent synthesis.

The reactions involving substituted cyclohexenes are much more complex than those involving cyclohexene itself. Addition of the carbene to 1,2-dimethylcyclohexene was expected to yield three products derived from the olefin-- the norcarane, and insertion products from the two different allylic positions. G.c. analysis of the reaction mixture showed only two materials of high retention times. Distillation of the reaction mixture failed to separate the two components, but relatively pure samples of each were obtained by preparative g.c. The microanalysis of the distilled mixture were in excellent agreement for a one to one adduct of carbene on the olefin, although the separated components had suffered some decomposition during partitioning and their analyses were somewhat less than perfect. Both components showed unsaturation to both bromine and permanganate. Both showed characteristic carbon-carbon double bond absorptions in the infrared. In addition, both showed two distinct carbonyl absorptions in the infrared. This feature appears to be characteristic of geminal diesters near a double bond. At this point, it appeared that the insertion products from the two different allylic positions had been isolated. The n. m. r. spectrum of one of the compounds showed peaks characteristic of methyl esters (τ 6.34) and malonyl proton (τ 6.50). The shifts of vinyl methyl groups and the ring protons were changed very little from those of the starting olefin. Integration of the n. m. r. signals correspond very well to the ratio calculated for compound (VII). However, the n. m. r. spectrum of the second component could not be rationalized in terms of an exo-

cyclic insertion product. The n. m. r. spectrum distinctly showed the presence of a vinyl proton (τ 4.60) and an aliphatic methyl group (τ 8.44). These features of the spectrum could only be explained on the basis of a rearranged product. Indeed, integration of the n. m. r. spectrum gave the ratio calculated for (VIII).

In the case of 1-methylcyclohexene, addition of the diazo compound was expected to give four products: cyclopropane and insertion products from the three different allylic positions. Analysis of the crude reaction mixture showed the presence of four components. Distillation of the crude mixture failed to separate the four compounds. However, microanalysis was consistent with a one to one carbene-olefin adduct. Relatively pure samples of each component were obtained by preparative g.c. As in the case of 1,2-dimethylcyclohexene, the adducts suffered some decomposition during separation, as shown by microanalysis. One of the compounds was saturated to bromine and to permanganate and was not destroyed by ozonolysis of the crude mixture. The n. m. r. spectrum showed the absence of vinyl protons but did show an aliphatic methyl group (τ 8.47). This compound was assigned the cyclopropyl structure (III).

The second fraction showed unsaturation to both bromine and permanganate. The infrared spectrum showed absorption due to C=C and two carbonyl bands. The n. m. r. pattern showed the presence of a vinyl proton (τ 4.79) and a vinyl methyl group (τ 8.34). The splitting pattern of the n. m. r. peaks due to the vinyl proton and the malonyl proton was identical to that observed for compound (II). Thus, the compound was assigned structure (VI).

The third component was unsaturated and showed two carbonyl bands

in the infrared. The n. m. r. spectrum showed a highly split vinyl proton and a doublet in the region of the malonyl proton. Integration of the n. m. r. signals approximated the ratio calculated for structure (IV). It should be pointed out that this was one of the least pure samples, as shown by carbon-hydrogen analysis.

The fourth component was found to be unsaturated, and showed two carbonyl bands in the infrared. The n. m. r. spectrum showed vinyl character (τ 4.54) and an aliphatic methyl group (τ 8.45). Integration of the n. m. r. signals corresponded to structure (V).

Chemical evidence for the above structural assignments was also obtained. Thus, addition of dimethyl diazomalonate to 3-methylcyclohexene resulted in the formation of small amounts of compounds V and VI in addition to the cyclopropane.

This observation nicely substantiates our earlier report that the dimethoxycarbonyl carbene is extremely selective and only inserts into the highest order C-H bond present.

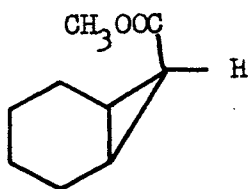
The frequently observed non-equivalence of the infrared spectra of the malonyl carbonyl chromophore is unusual. We suspect this is a consequence of overlap between C=C and π^* orbitals with the n and/or π^* orbitals in one carbonyl group. Such behavior is not observed with malonic esters where the groups should be equivalent and no C=C bond is present.

Interaction of Nucleophiles with 7,7-Dimethoxycarbonylnorcarane

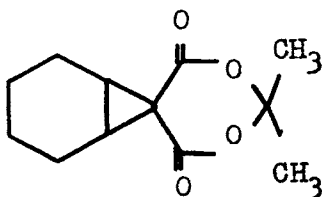
7,7-Dimethoxycarbonylnorcarane was subjected to Michael-type reaction conditions using a wide variety of solvents, nucleophiles, and temperature conditions. The norcarane showed remarkable stability

under such conditions, and no indications of a ring-opening reaction was observed. In most cases, 90% or more of the unchanged norcarane was recovered from the reaction mixtures. The resistance of the norcarane to these reaction conditions probably reflects a steric problem. The approach of the nucleophile is blocked on one side by the six-membered ring and on the other side by the ester groups. For that reason, several small nucleophiles were tried in addition to the synthetically more desirable malonate. These efforts were also unsuccessful.

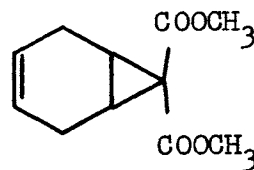
The steric problem is not insurmountable and there exists at least three possible solutions to the problem. These possibilities are based on compounds (3), (4), and (5). The use of 7-endo-methoxycarbonylnorcarane (3) would essentially remove the steric factor to



(3)



(4)

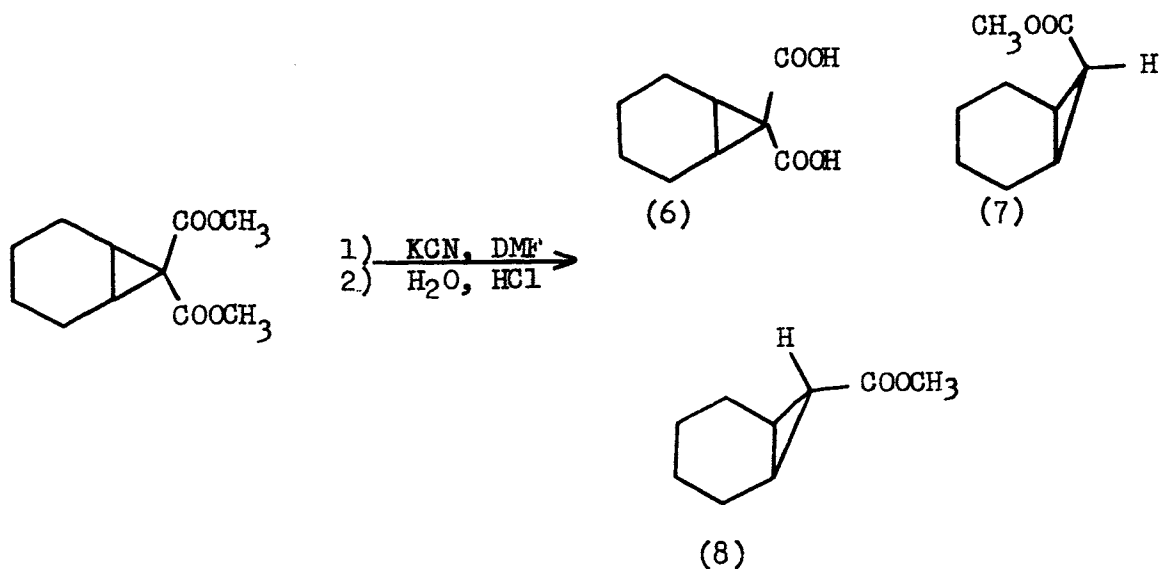


(5)

the approaching nucleophile. While the sacrifice of one ester function would make the Michael reaction electronically less feasible, the steric factor is probably more important. The isopropylidene (4) is electronically more attractive but does not offer complete freedom from steric interference. Freezing the configuration of the cyclohexane ring by the introduction of a double bond (5) might also

increase the likelihood of attack on the cyclopropane.

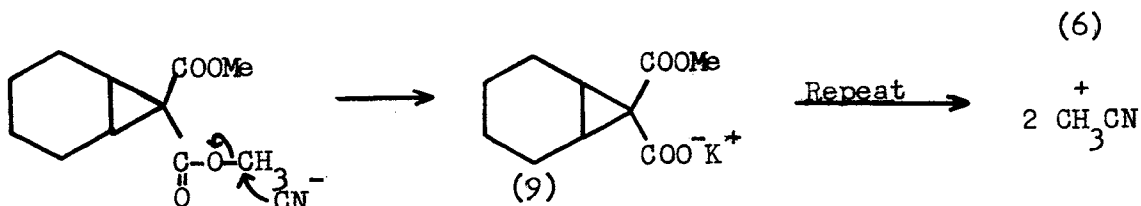
Although the attempted Michael reactions were unsuccessful in connection with the original synthetic scheme, two interesting and useful reactions were discovered. One of these, the transesterification, was discussed previously.⁶ The second involves hydrolysis of 7,7-dimethoxycarbonylnorcarane by potassium cyanide in dimethylformamide. This reaction gave the corresponding diacid (6) along with the mono esters (7) and (8).



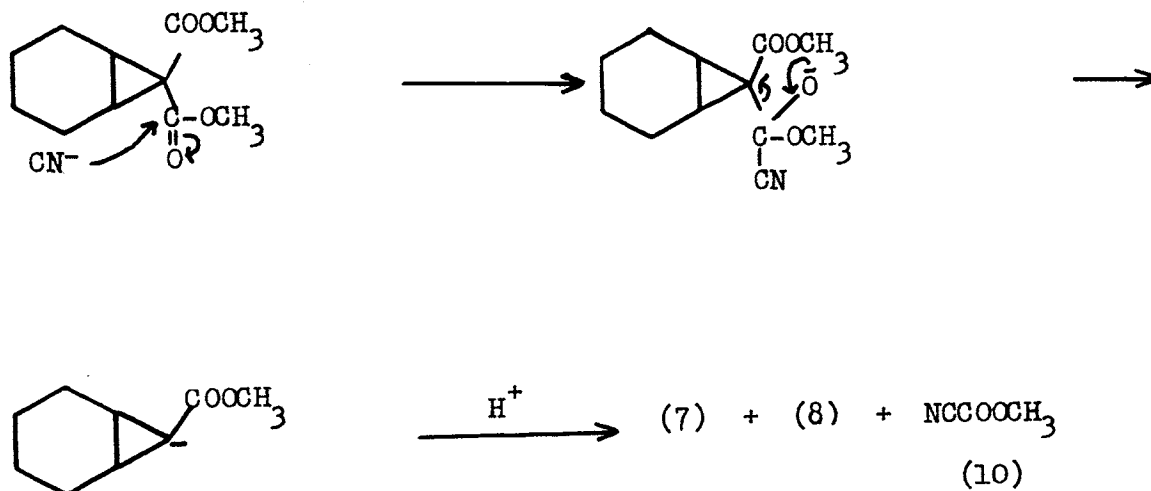
The cleavage of the alkyl oxygen bond of methyl esters via nucleophilic displacement of carboxylate anion from the methyl group by lithium iodide in amines is well known.²⁶ In addition, Krapcho²⁷ has reported that reaction of geminal diethyl esters with sodium cyanide in dimethylsulfoxide gives the mono ester, and Johnson²⁸ has reported B_{AL2} type cleavage of esters with lithium n-butyl sulfide. Krapcho's yields were on the order of 80% but no mention was made of other products. Dolby²⁹ modified Krapcho's method by substituting dimethyl-

formamide as solvent.

No effort was made to elucidate the exact mechanism of the potassium cyanide hydrolysis. It appears to involve two competing processes, possibly as represented in schemes (1) and (2). None of



Scheme 1



Scheme 2

the acid corresponding to (9) was isolated, indicating that the anion of (9) somehow facilitates the second step. The absence of the hydrocarbon (norcarane) indicates that scheme (2) is not repeated. This may be due to consumption of all cyanide. Assuming its formation, ester (10) would be expected to react rapidly with cyanide ion. This assumption accounts for all the available cyanide. The possibility of

(7) and (8) arising by decarboxylation of (9) would not account for the lack of norcarane formation.

The fate of the ester carbon was briefly pursued and it was observed that no acetonitrile was present at the end of the reaction. Treatment of acetonitrile under the reaction condition led to its consumption, presumably in a Thorpe condensation. Dolby³⁰ also failed to find any nitrile at the end of his reactions.

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VITA

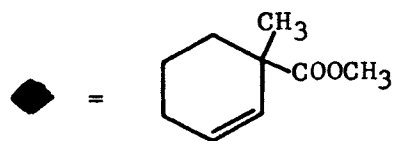
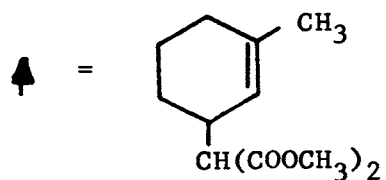
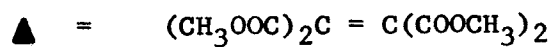
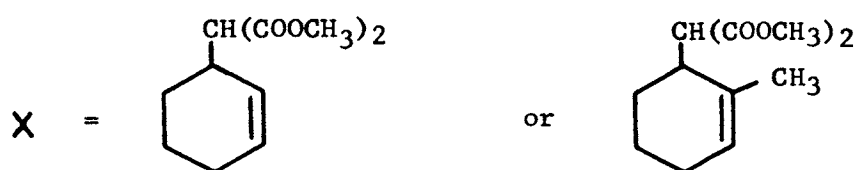
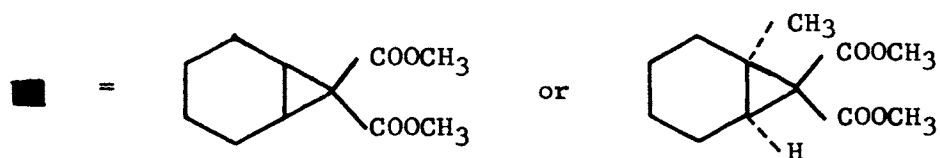
Billy Wayne Peace was born August 22, 1944 in Williamsburg, Kentucky. He received his primary and secondary education in Williamsburg, Kentucky. He received his Bachelor of Arts degree with a major in chemistry from Berea College, Berea, Kentucky in June, 1966. He entered Tennessee Technological University, Cookeville, Tennessee in September of 1966 and received his Master of Science degree with a major in organic chemistry in June, 1968.

He has been enrolled in the Graduate School of the University of Missouri-Rolla since September, 1968 and has held a teaching assistantship in the Department of Chemistry during this time. He also received support from a NSF Grant during the summer of 1971. He received his Ph. D. degree in organic chemistry in December, 1971.

APPENDIX A

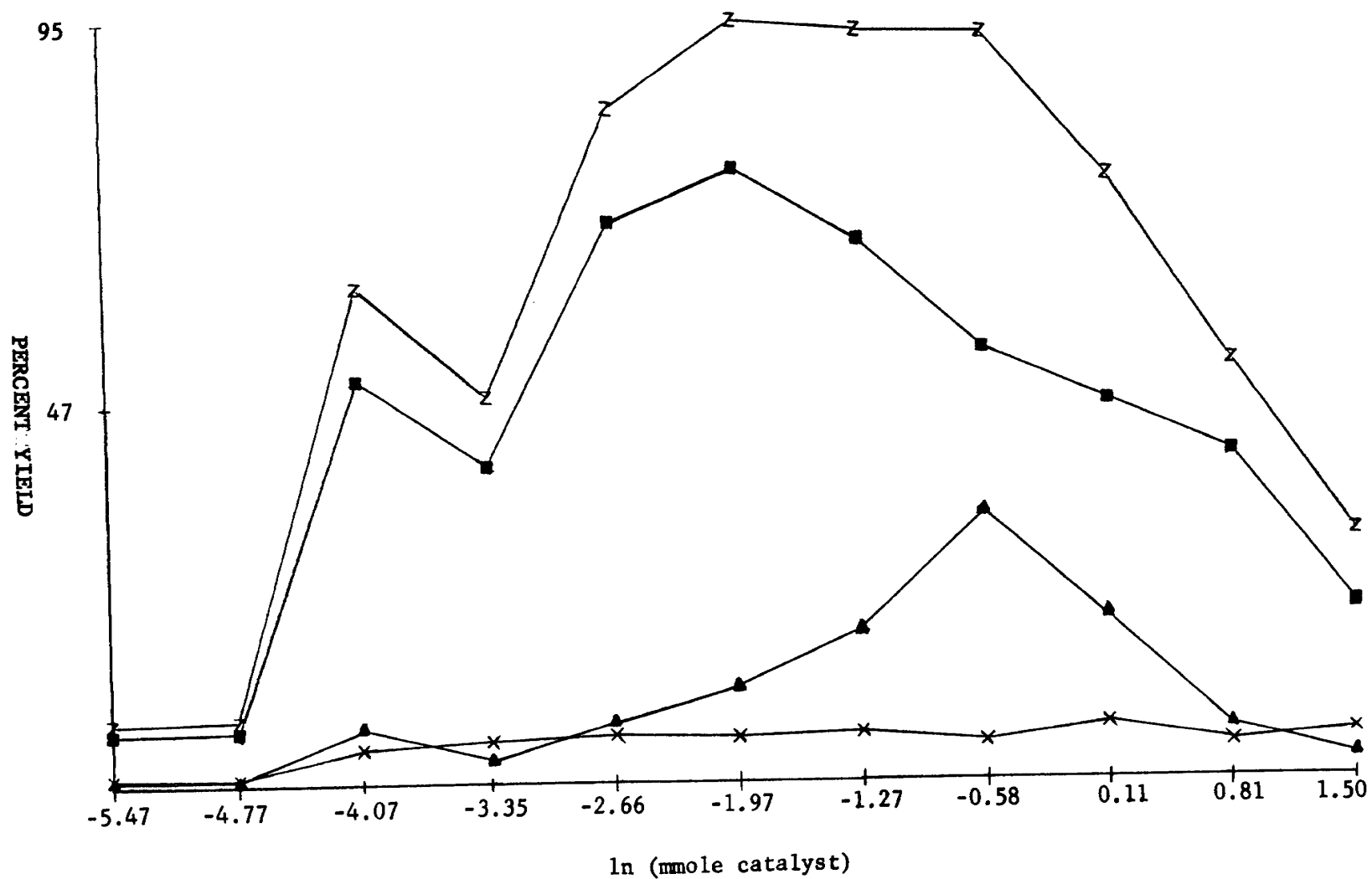
GRAPHICAL PRESENTATIONS OF DATA

Throughout appendix A, the compounds below will be assigned the following symbols.

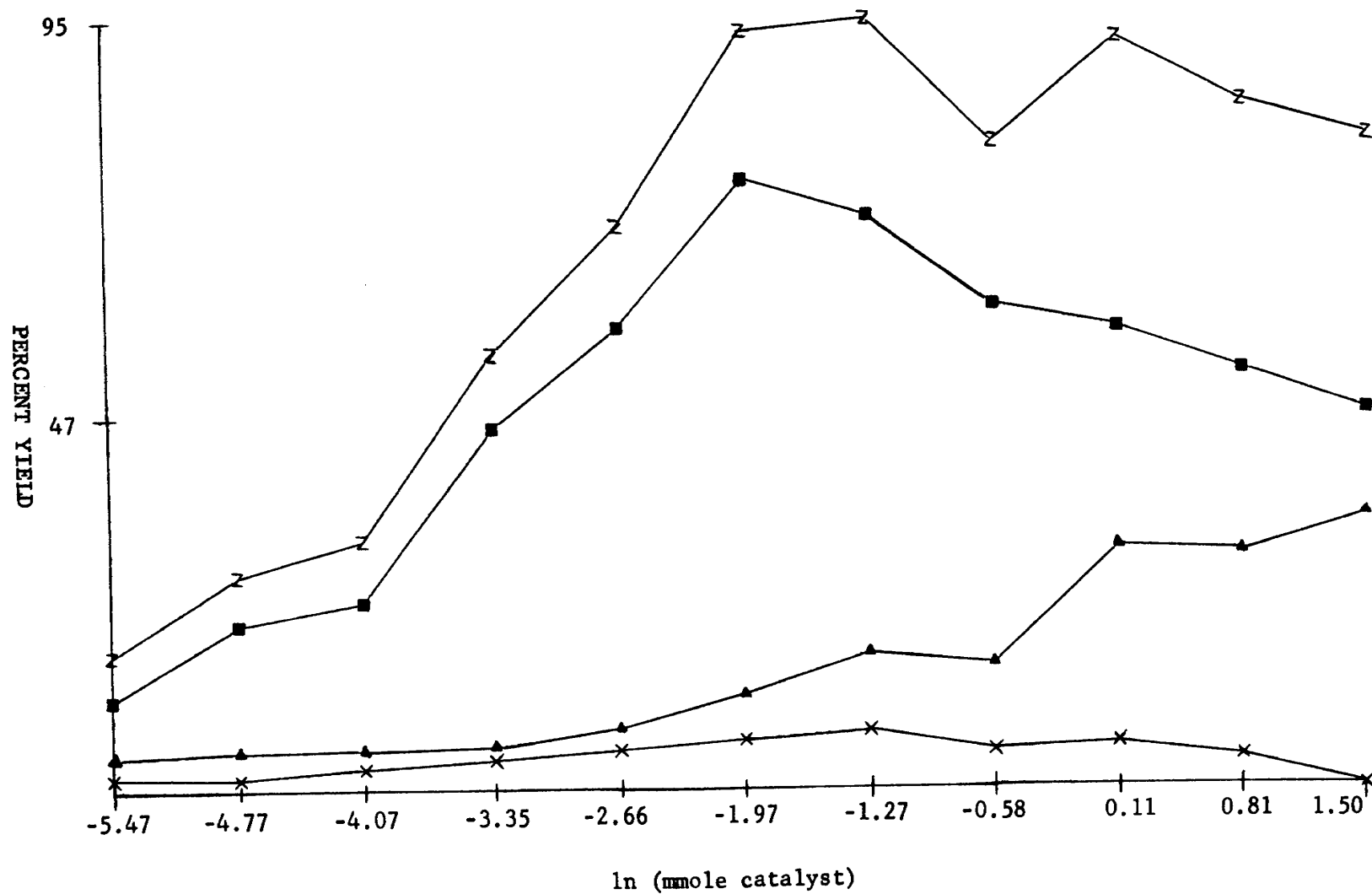


⌘ = Total Insertion

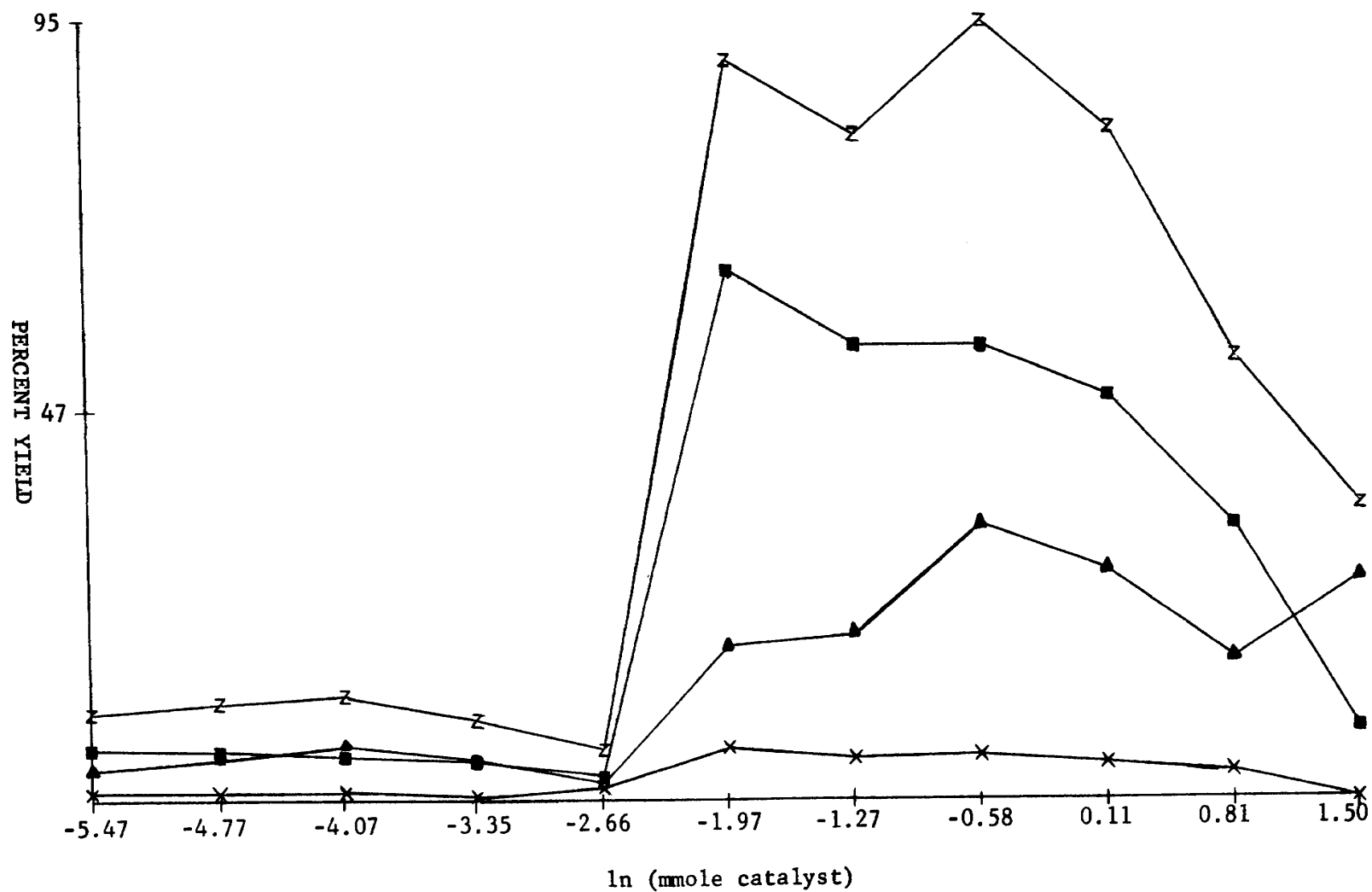
⌘ = Total Product



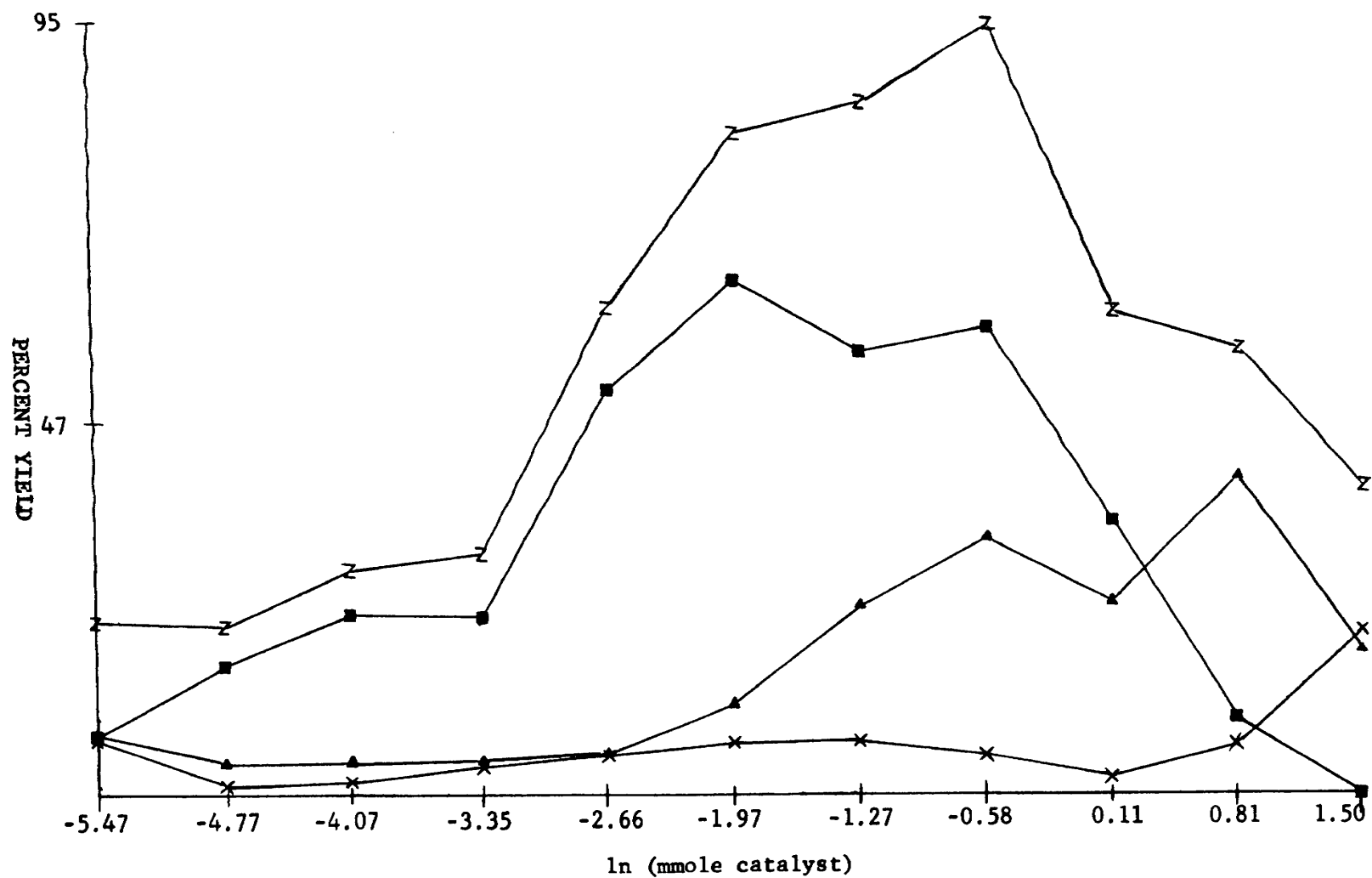
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $\text{Cu}(\text{AcAc})_2$ CONCENTRATION
IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



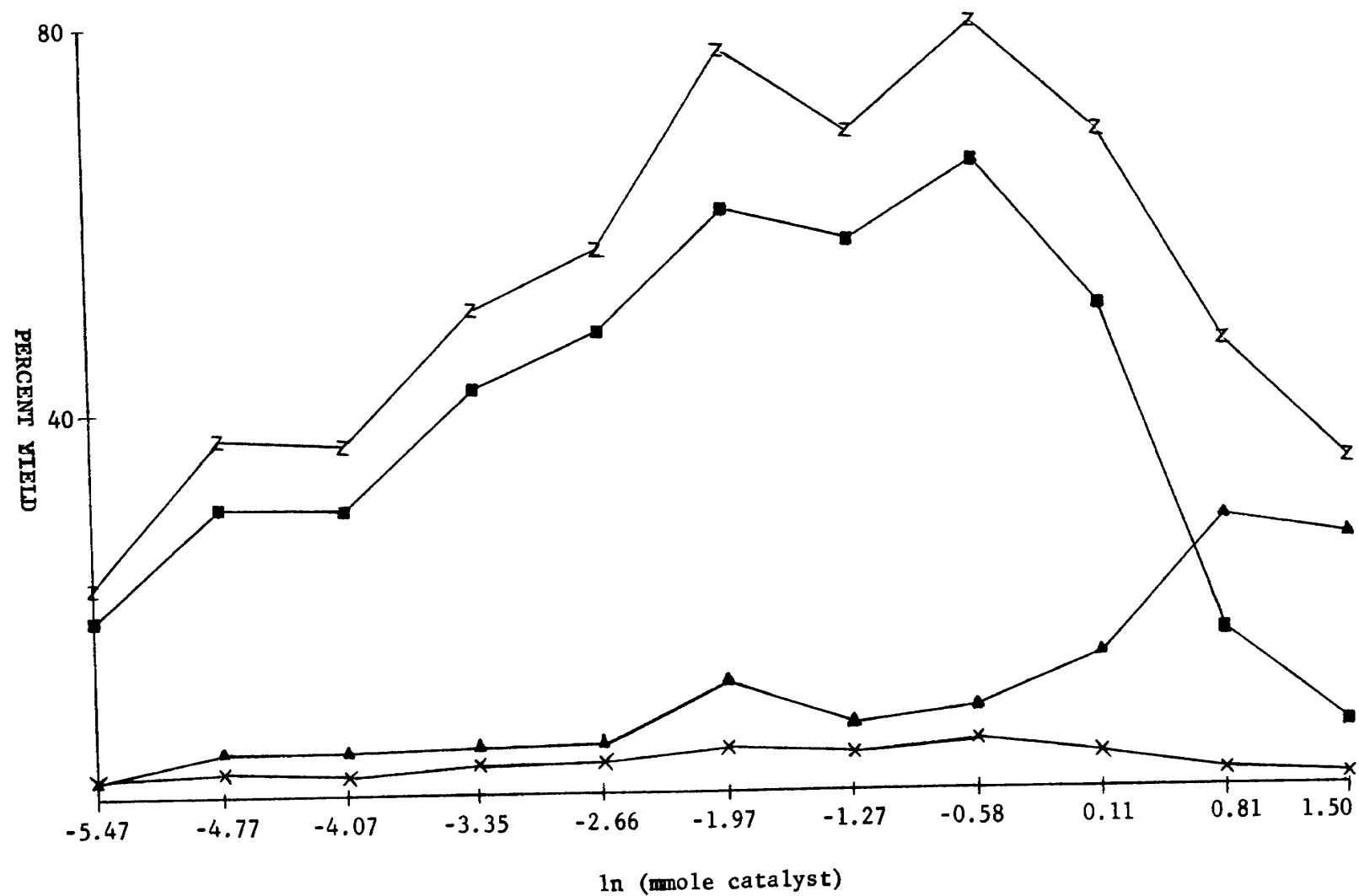
PRODUCT DISTRIBUTION AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuI}$ CONCENTRATION
IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



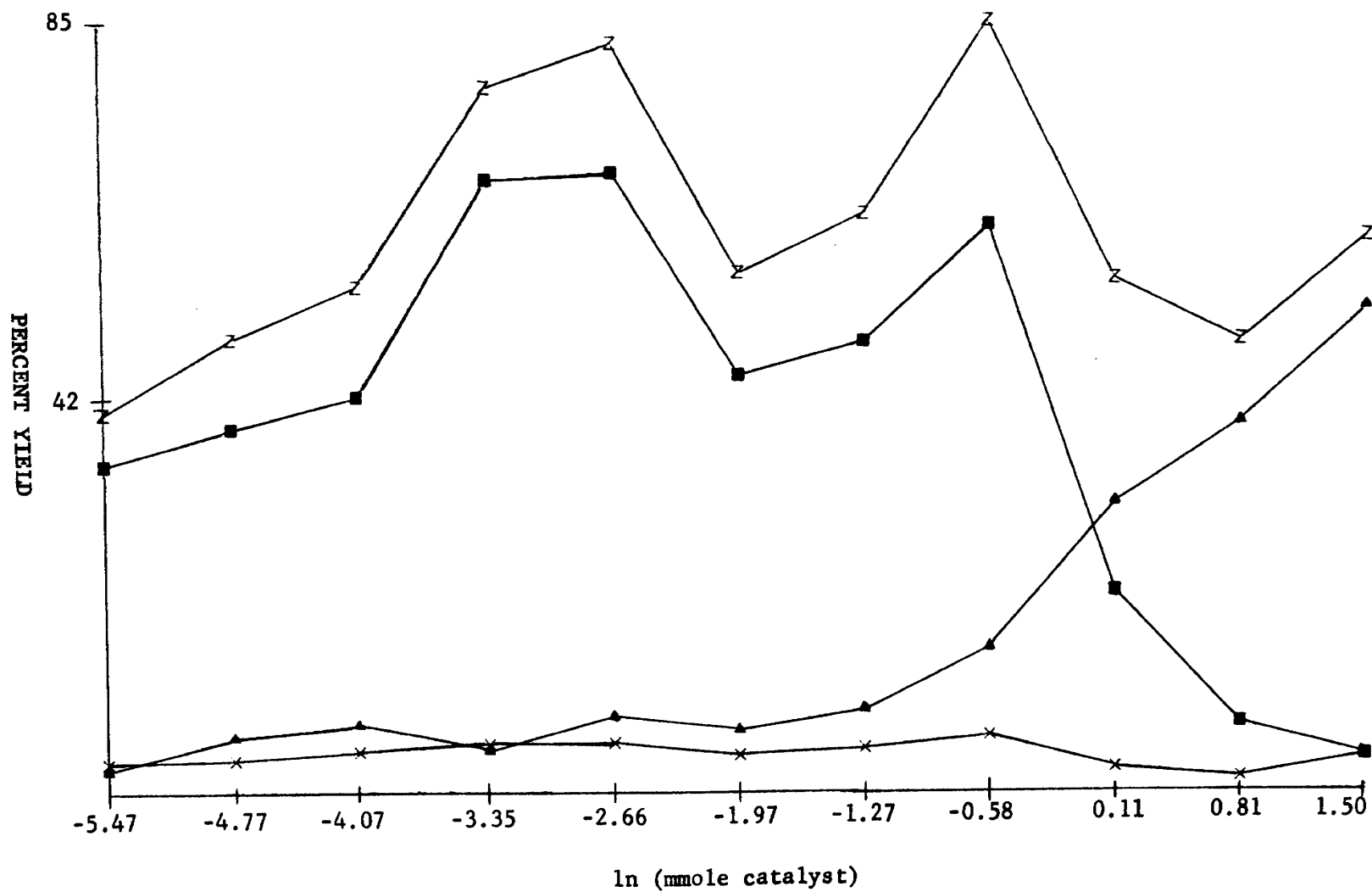
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $[(\text{CH}_3\text{O})_3\text{P}]_2\text{-CuI}$ CONCENTRATION
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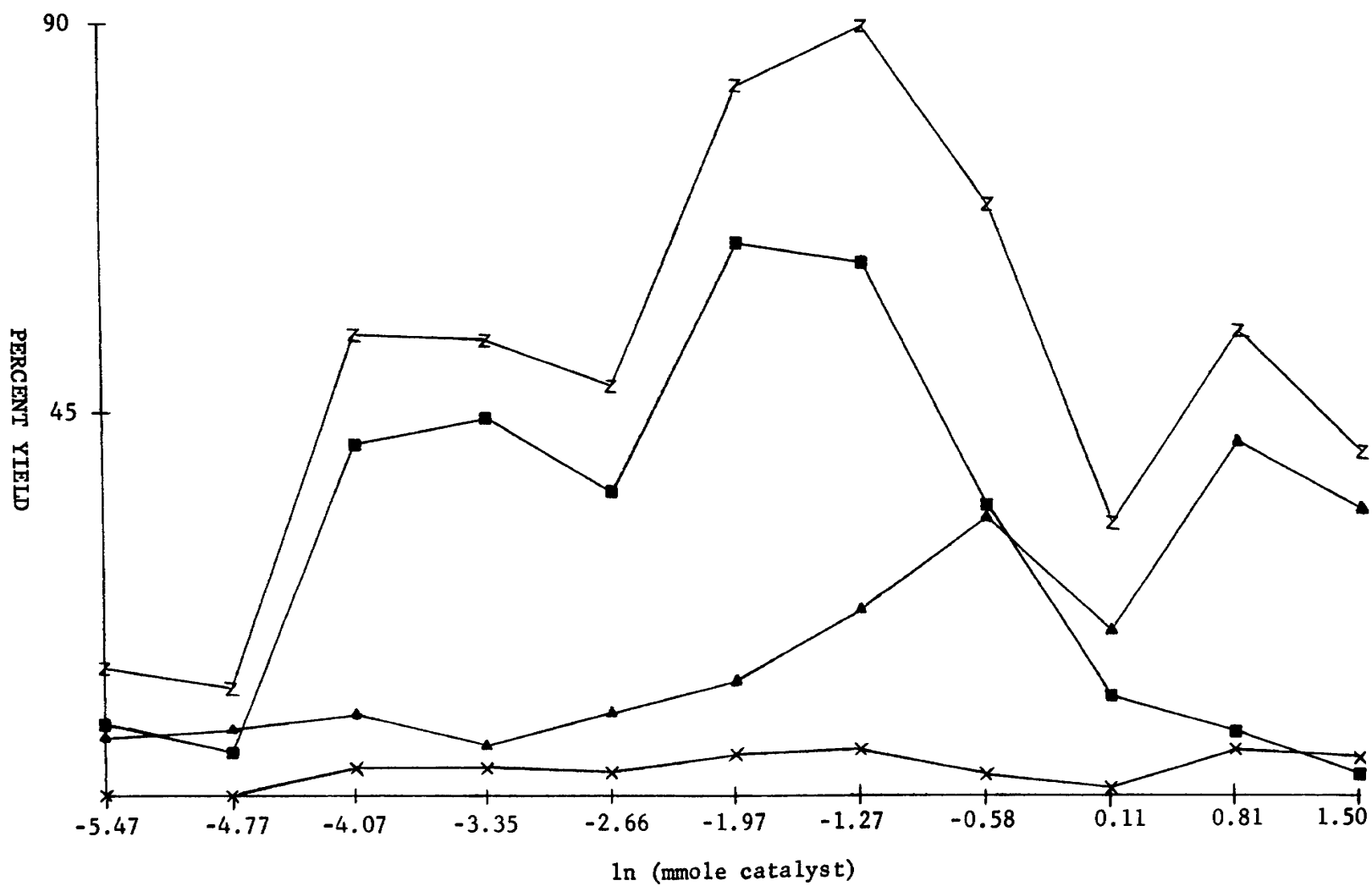
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IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



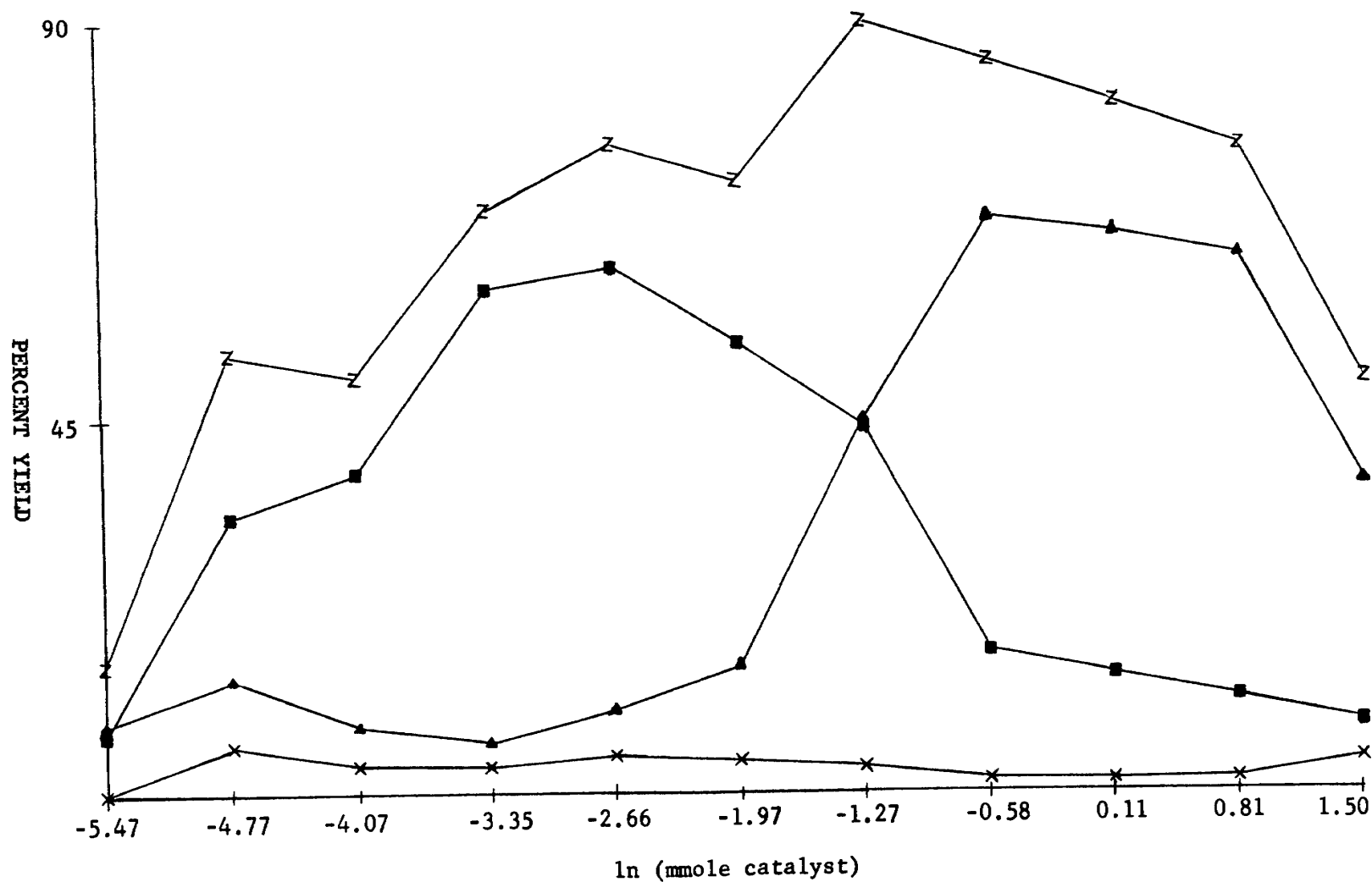
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF (1-Pro-O)₃-P-CuCl CONCENTRATION
IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



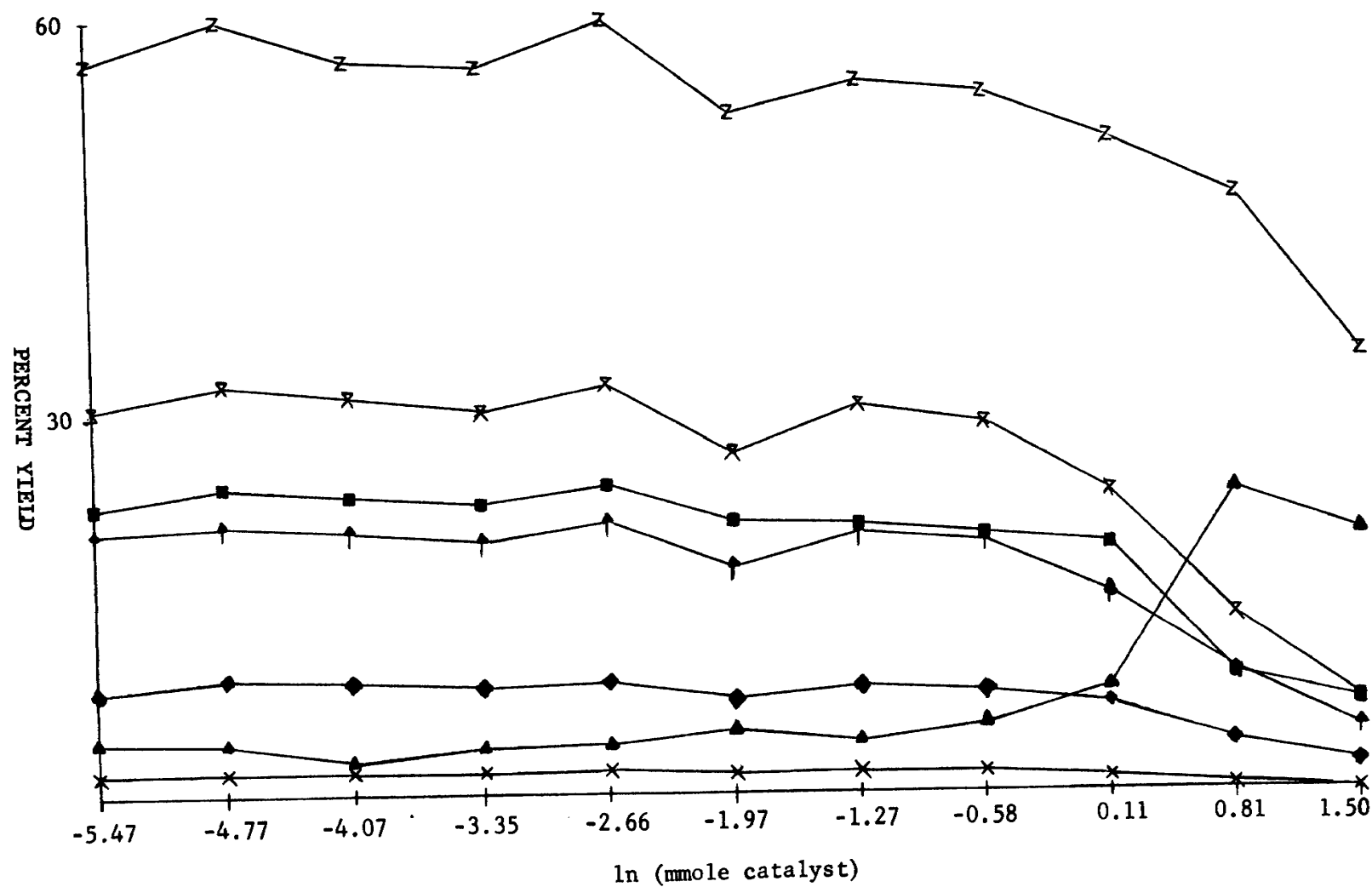
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ (METHOD A)
CONCENTRATION IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



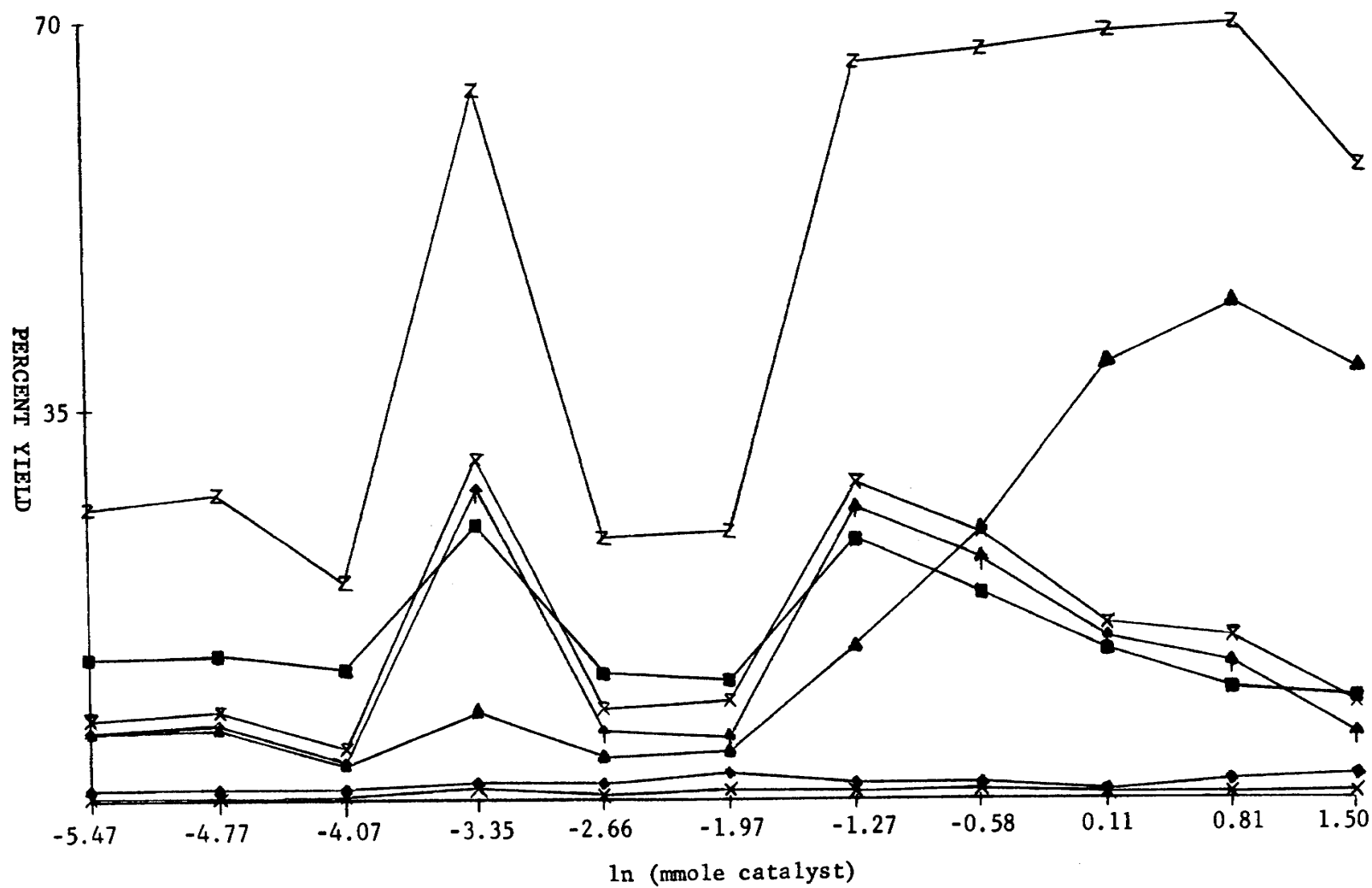
PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ (METHOD B)
CONCENTRATION IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



PRODUCT DISTRIBUTION AND YIELDS AS A FUNCTION OF $(\text{CH}_3\text{O})_3\text{P-CuCl}$ (METHOD C)
CONCENTRATION IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH CYCLOHEXENE



PRODUCT DISTRIBUTION AND YIELDS IN THE REACTION OF DIMETHYL DIAZOMALONATE
WITH 1-METHYLCYCLOHEXENE USING $(\text{CH}_3\text{O})_3\text{P-CuCl}$ AS CATALYST AT 110°C



PRODUCT DISTRIBUTION AND YIELDS IN THE REACTION OF DIMETHYL DIAZOMALONATE WITH 1-METHYLCYCLOHEXENE
 USING $(\text{CH}_3\text{O})_3\text{P-CuCl}$ AS CATALYST IN REFLUXING HEXAFLUOROBENZENE AT 83°C (90 mole per cent HFT)

APPENDIX B

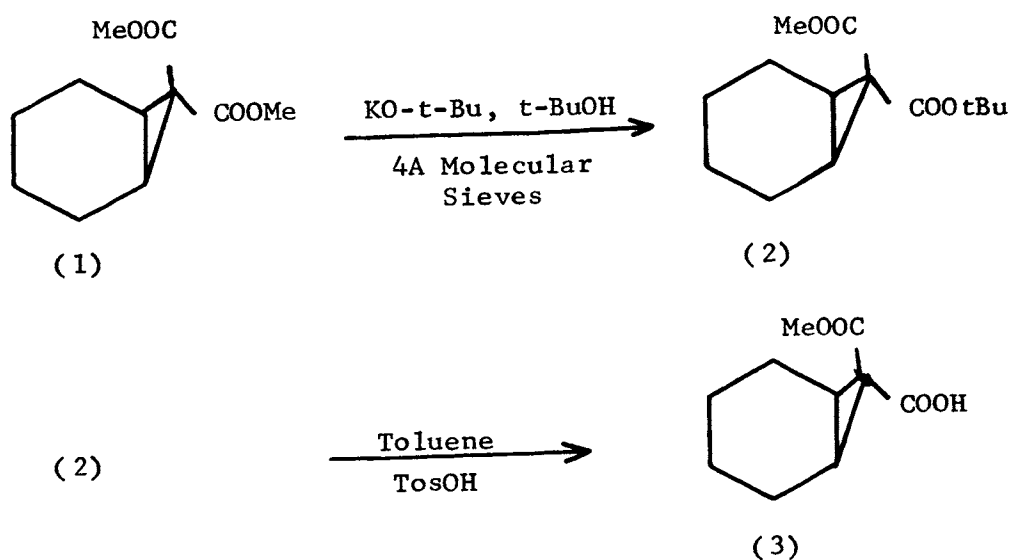
PUBLICATION PREPRINTS AND REPRINTS

Synthesis, 1971 (In press)

Preparation and Use of *t*-Butyl Esters: Selective Transesterification

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 Department of Chemistry
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 Rolla, Missouri 65401

Musso¹ has reported that the room temperature hydrolysis of 7,7-dicarboethoxy norcarane leads to the 7-exo-carboxy-7-endocarboethoxy norcarane in 73% yield. We have developed a two step procedure which gives this transformation in almost quantitative yield. Thus, treatment of 7,7-dicarbomethoxy norcarane (1) with potassium *t*-butoxide in the presence of 4-A molecular sieves gives the mixed ester (2). In the absence of molecular sieves this reaction stops



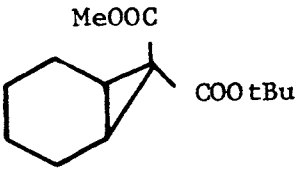
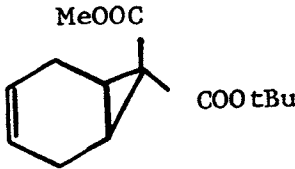
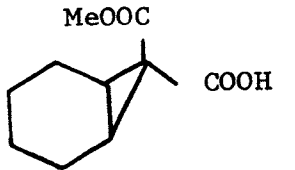
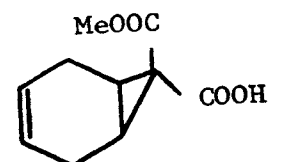
at 80% conversion and cannot be forced to completion by excess base or longer reaction time. Instead of using molecular sieves, the reaction can be completed by removing the solvent and adding fresh *t*-butyl

*To whom inquiries should be addressed

alcohol twice. Also, the reaction can be carried out with less than an equivalent of base but much longer reaction times are required.

The conversion of (2) to (3) can be carried out without the actual distillation of the mixed ester. Both steps of this sequence were shown by g.c. analysis to be quantitative and clean. The yields given in the table reflect mechanical loss.

The structure of the products were established by n.m.r., IR and C-H analysis. The configuration of C-7 was confirmed by decarboxylation to the corresponding endo-esters and interrelation by hydrogenation of the 7-endo-carbomethoxy norcar-3-ene.

	B.P.	M.P.	% yield
	76-78°C /0.01mm	39.5- 40.5°C	97%
	76-78°C /.005mm		94%
		112-114°C	96%
		126-7°C Cor.	98%

Procedure:

7-exo-carbo-t-butoxy-endo-carbomethoxy norcarane: A solution of 21.2 g (0.1 mole) of 7-7-dicarbomethoxy norcarane and 11.2 g (0.1 mole) of potassium t-butoxide in 400 ml of dry t-butyl alcohol was warmed to about 40°C under nitrogen. After 12 hours, the solvent was removed using a Büchi rotovaporator with a calcium chloride drying tube in the aspirator line and replaced with fresh t-butyl alcohol. To this solution was added 15 g of 4A molecular sieves and the mixture allowed to stand, without stirring, for an additional 24 hours. The mixture was filtered, 200 ml of water added and the solution neutralized with dilute HCl. After removal of the t-butyl alcohol, the organic layer was separated and the aqueous layer extracted three times with ether. The combined organics were washed with water, sat. NaCl solution then dried over anhydrous sodium sulfate. After removal of the ether, the oil was distilled to give 24.6 g (97%) of the colorless mixed ester. The product can be crystallized from methanol. The reaction can be worked up after the initial 12 hours since the mixed ester is easily separated from the dimethyl ester by vacuum distillation.

7-exo-carboxy-7-endo-carbomethoxy norcarane: A solution of 2.54 g (0.01 mole) of the above mixed ester and 5 mg anhydrous p-toluene-sulfonic acid in 15 ml of dry toluene² was heated at reflux. A gas was evolved which rapidly decolorized Br₂/CCl₄ (isobutylene). Reflux was continued until no more gas was generated, about 3 hours. The solution was cooled, and the volume of solvent reduced to about 5 ml. On further cooling, crystals formed. After filtering and drying, 1.90 g (97%) of the acid was collected. The melting point was not improved by recrystallization.

References

- 1) H. Musso, Chem. Ber., 101, 3710 (1968).
- 2) G. S. Fonken & W. S. Johnson, J. Amer. Chem. Soc., 74, 831 (1952).
- 3) This work was supported in part by NSF Grants GP-3768 and GY-3514.

Tetrahedron Letters, 3799(1971).

Tetrahedron Letters No. 41, pp 3799 - 3802, 1971. Pergamon Press. Printed in Great Britain.

SOME OBSERVATIONS OF THE EFFICACY OF SOLUBLE COPPER(I) CATALYSTS FOR DECOMPOSING DIAZO COMPOUNDS

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(Received in USA 22 July 1971; received in UK for publication 7 September 1971)

Moser¹ has described studies employing soluble copper(I) catalysts for the decomposition of diazoacetic ester in the presence of olefins and Dave and Warnhoff² have given additional details including directions for purification of the catalysts.

There are however several important points of immediate synthetic utility which are not covered in the literature. We have observed the behavior of these catalysts systems with diazomalonic esters³ which extrapolates to diazoacetic ester and probably to most, if not all, diazo compounds.

Concentration and Precautions: Moser employed relatively large amounts of catalyst, degassed his systems and used peroxide free olefins. These precautions, although desirable for mechanistic studies, are both unnecessary and undesirable for mechanical and chemical reasons during synthetic studies. Thus, the addition of small amounts of radical initiators such as benzoyl peroxide (preferably) or azo-bis-isobutyronitrile (Vazo^{®4}) to carefully purified olefins leads to cleaner reactions and higher yields. It also permits using as little as 0.14 mmole of catalyst to decompose 20 mmole of diazo compound whereas Moser had to employ 5.0 mmole. We have determined that the carbenoid process is not radical initiated but rather involves a change of catalyst.⁵ Commercial cyclohexene freshly distilled from sodium contains sufficient impurities to promote increased catalyst activity whereas filtration through fresh activated alumina⁶ necessitates employing larger quantities of catalyst.

The yields from such reactions are very dependent upon the catalyst concentration, Chart 1 being typical. This is also true of diazoacetic ester (Table 1). A wide range of isomer ratios is obtained by adjusting catalyst concentrations.⁷

Purification of Catalysts: The purification of the catalysts is occasionally desirable. However, if halogenated solvents are employed in recrystallization either singly or with

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TABLE 1

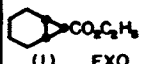

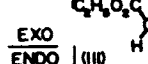
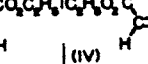

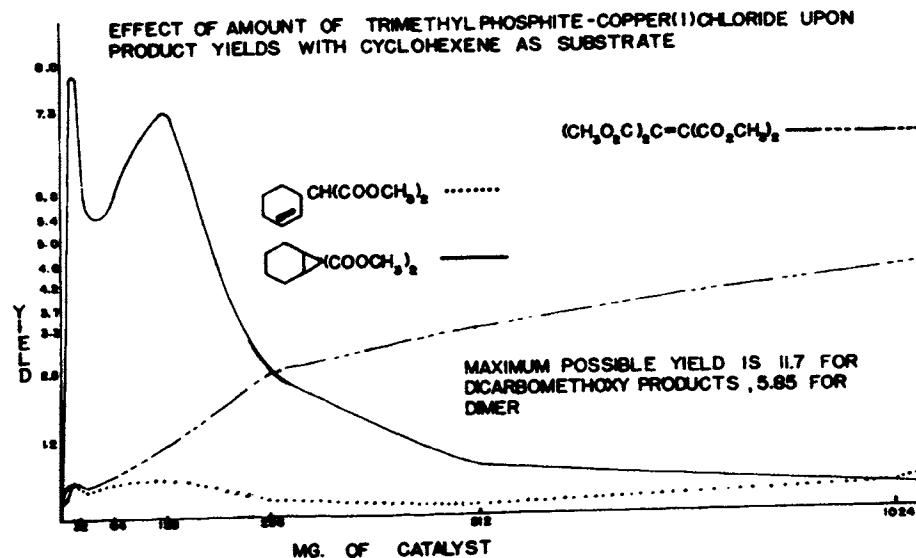
PRODUCT DISTRIBUTION FROM THE REACTION OF CYCLOHEXENE, DIAZOACETIC ESTER CATALYZED BY COPPER(I)IODIDE·N=P(OCH ₃) ₃ AS A FUNCTION OF N AND CATALYST CONCENTRATION AT 85°										
MMOLE OF CAT. AND N	PRODUCTS AND YIELDS									
	(I) 	(II) 								CIS TRANS
	ABSOLUTE	RELATIVE	ABSOLUTE	RELATIVE	RATIO	ABSOLUTE	RELATIVE	ABSOLUTE	RELATIVE	RATIO
N=1										
0.14	7.80	1	0.65	0.083	12.0	0.088	0.011	0.123	0.015	0.715
5.0	2.91	1	1.16	0.390	2.51	0.218	0.075	0.710	0.244	0.307
N=2										
0.14	7.87	1	0.684	0.087	11.5	0.100	0.012	0.150	0.019	0.667
5.0	0.965	1	0.946	0.980	1.02	0.077	0.079	0.254	0.263	0.304
N=3										
0.14	8.05	1	0.533	0.066	15.1	0.067	0.008	0.111	0.013	0.608
5.0	0.333	1	0.832	2.50	0.400	NONE		NONE		

CHART 1

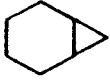
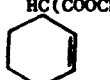


The data in Chart 1 and Tables 1 and 2 was obtained in the following way. A solution of 0.02 mole of diazo compound in 25 ml of cyclohexene (distilled from and stored over sodium) was added to 25 ml of refluxing olefin containing the catalyst. The yields were determined by v.p.c. and are relative to an internal standard. Diazo compounds were carefully distilled to 98.5-99% purity. Traces of chloroacetic ester may interact with the catalysts but clearly different effective catalysts are present in the 3 cases of Table 1.

co-solvents, appreciable destruction of the catalyst can occur. This involves reaction between the phosphite and the halogenated solvent and leads to precipitation of some of the copper(I) salt.⁸ Catalysts resulting from this type of treatment contain varying amounts of uncomplexed salt and are less effective than pure material (Table 2).⁹

Table 2

Product Distribution in the Reaction of Cyclohexene with Dimethyl Diazomalonate

CATALYST 0.14 mmole	 $(\text{COOCH}_3)_2$		$(\text{CH}_3\text{OOC})_2\text{C}=\text{C}(\text{COOCH}_3)_2$		 $\text{HC}(\text{COOCH}_3)_2$	
	ACTUAL	RELATIVE	ACTUAL	RELATIVE	ACTUAL	RELATIVE
I $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuI}$	8.57	1.00	0.930	0.108	0.697	0.081
II $(\text{CH}_3\text{O})_3\text{P} \cdot \text{CuI}$	7.67	1.00	1.55	0.202	0.767	0.100
III $(\text{CH}_2\text{O})_3\text{P} \cdot \text{CuI}$	7.40	1.00	0.906	0.122	0.760	0.103
IV $(\text{CH}_3\text{O})_3\text{P}\cdot\text{CuCl}$	7.45	1.00	1.07	0.144	0.547	0.070
V IV plus 30 mg CuCl	3.90	1.00	2.70	0.692	0.276	0.071
VI IV plus 30 mg CuCl_2	6.41	1.00	1.45	0.223	0.623	0.097

The phosphite ligand serves as a solubilizing substituent for the copper species but has a deleterious contribution to the overall reaction because of phosphinazine formation.¹⁰ The phosphinazines are readily decomposed under the reaction conditions, both thermally and catalytically.¹⁰ However, the products resulting from the decomposition of the phosphinazine bear no resemblance to the identifiable products of the carbenoid processes.¹¹

Table 2 shows the presence of phosphite does have a deleterious effect for diazomalonate and the contribution is not linear. Formal addition of 0.14 mmole increments of phosphite to 0.14 mmole of the mono complex (the bis and tris complexes result) causes a decrease in norcarane yield of approximately 0.9 and an additional 0.3 mmoles. The presence of added copper(I) chloride would be expected to have a slight beneficial effect resulting from reducing the concentration of phosphite because of low solubility. A more deleterious contribution results from the increased common anion. The resultant mixture serves as only a fair catalyst for the desirable processes. The use of copper(II) chloride leads to destruction of the phosphite¹² and any residual copper(II) salt furnishes lesser quantities of anion¹³ because the central atom is more highly charged and hence less prone to ionization.^{14,15}

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Acknowledgments: This work was supported in part by the National Science Foundation in the form of equipment grants, GP-3768 and GP-3514.

References and Footnotes

1. W. R. Moser, J. Amer. Chem. Soc., **91**, 1135, 1141 (1969).
2. V. Dave and E. W. Warnhoff, "Organic Reactions", Vol. 18, Wiley, New York, N.Y., 1970, p 217.
- 3a. D. S. Wulfman, F. C. Carman, B. G. McGiboney, E. K. Steffen and B. W. Peace, Preprints, Division of Petroleum Chemistry, ACS, **16** (1), B81 (1971) (b) D. S. Wulfman, E. K. Steffen and B. W. Peace, 161st National ACS Meeting, Organic Division, Los Angeles, March 28-April 2, 1971. (c) Further details are to be published elsewhere.
4. Trademark, E. I. du Pont de Nemours & Company.
5. The exact nature of the new catalyst system is currently under investigation. Olefins containing small amounts of peroxides also require much less catalyst although the reactions are not as clean.
6. Alumina filtration has been found to be an efficient means for complete removal of small to moderate quantities of peroxy impurities in hydrocarbons. See Waters Associates Inc., Application Note 105, "Purification of Solvents by Active Alumina."
7. Moser observed an exo-endo ratio range of 6.86 to 5.93 operating in the temperature range 30 to 70°C.
8. The reaction of halocarbons with phosphines is a well recognized reaction both for the formation of phosphonium salts and for halogenation of alcohols to the corresponding halides. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N.Y., 1968, p 1247.
9. The catalyst preparation given in reference 2 was modified. Thus, after removal of the benzene, methanol was added, the mixture cooled and filtered. Catalysts obtained in this way were shown to be pure by m.p., n.m.r. and elemental analysis.
10. For a review of the preparation and decomposition of phosphinazines see A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N.Y., 1966, p 238.
11. D. R. Dalton and S. A. Liebman, Tetrahedron, **25**, 3321 (1969), have reported that diphenylmethylene is obtained from the decomposition of a related phosphinazine.
12. We have found the reaction of copper(II) chloride with 2 equivalents of trimethylphosphite in benzene is a convenient means of preparing trimethylphosphite copper(I) chloride.
13. We have found the counter ion when introduced from an alternate source drastically depressed the formation of cyclopropane, insertion product and carbene dimer.
14. Mechanistic details appear in two papers, B. W. Peace and D. S. Wulfman, J. Chem. Soc. (D), (in press).
15. Experimental details appear in B. W. Peace and D. S. Wulfman, Synthesis (in press). We will furnish on request.

Chemical Communications, 1179(1971).

The Effect of Peroxides on the Reactions of Dimethoxycarbonylcarbene Generated with Soluble Catalysts from Dimethyl Diazomalonate

By B. W. PEACE and D. S. WULFMAN*

(Department of Chemistry, University of Missouri - Rolla, Rolla, Missouri 65401)

Summary The presence of alkenyl or aryl radicals converts trimethyl phosphite copper(I) iodide into an extremely potent soluble catalyst capable of decomposing diazo-esters cleanly into the corresponding carbenoid species.

For the past several years we have been examining the copper- and copper salt-catalysed decomposition of dimethyl diazomalonate in the presence of some cyclic olefins.¹ The report by Moser² that soluble catalysts of the type trialkyl phosphite copper(I) halide are excellent catalysts for decomposing diazoacetic ester led us to extend his studies to dimethyl and di-*t*-butyl diazomalonates. These studies revealed that under optimum conditions soluble catalysts lead to nearly doubled yields (compared to heterogeneous catalysts), there is a dependence upon catalyst concentration,³ and that the nature of the counterion influences the overall yields and product

distributions.⁴ When this is coupled with the effect of added counterion, it becomes clear that the rate-determining step involves displacement of the anionic ligand by diazo-compound.⁴

Although individual batches of olefin behave in a consistent manner, there were large variations in product distributions and yields depending upon which batch of olefin was employed and how it was purified and stored. In addition, we found that we obtained better results than Moser using his system but operating at lower catalyst concentrations. Surprisingly, Moser's catalyst concentration led to very poor results. There was, however, one major difference between the two studies. We did not filter our olefin through alumina[†] immediately prior to undertaking a reaction as Moser had. When such precautions were undertaken for our system the results were worse than if no catalyst had been employed. We concluded that peroxy impurities in the olefin greatly enhance

[†] It has been reported that alumina filtration removes peroxy impurities from hydrocarbons. See Waters Associates Inc., Application Note 105, "Purification of Solvents by Active Alumina."

TABLE

Product distribution and yields in the reaction of cyclohexene and dimethyl diazomalonate as a function of catalyst and peroxide content of the olefin

		% Yield			
(CH ₃ O) ₂ P-CuZ 0.14 mmole		(I)	(MeO ₂ C) ₂ C: C(CO ₂ Me) ₂	(II)	Ratios
Z = Br ^a	..	68.7	15.1	6.66	1.00:0.219:0.097
I ^a	..	74.3	12.9	7.43	1.00:0.174:0.100
Br ^b	..	22.0	1.88	2.08	1.00:0.085:0.095
I ^b	..	19.9	2.02	1.79	1.00:0.101:0.090
Br ^c	..	71.6	22.9	5.72	1.00:0.320:0.080
I ^c	..	78.8	15.0	5.92	1.00:0.191:0.075
No Catalyst ^c	..	9.45	1.82	0.00	1.00:0.192

^a Commercial cyclohexene.

^b Commercial cyclohexene filtered through alumina.

^c Commercial cyclohexene filtered through alumina, then 0.07 mmole benzoyl peroxide added.

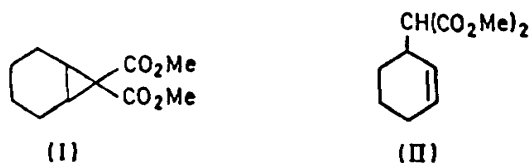
All reactions were run as follows: A solution of 0.02 mole of dimethyl diazomalonate in 0.25 mole of cyclohexene was added at the rate of 6 drops per min to 0.25 mole of refluxing olefin containing the catalyst or catalyst plus peroxide. After 24 h at reflux, the excess of olefin was removed by distillation, and the residue analysed by g.l.c. using diglyme as an internal standard.

catalyst activity. This is nicely supported by comparable experiments carried out with the addition of benzoyl

in benzene prior to the addition of olefin or diazo-compound a catalyst far superior to any previously observed is obtained. It therefore seems extremely unlikely that the catalytic decomposition of diazo-compound is proceeding in a radical manner initiated by peroxides and that triplet carbenoid is therefore not an artifact. The inescapable conclusion is that the hydrocarbon and/or benzoyl radicals react with the catalyst to generate new catalysts which are superior to the material added. We are currently investigating the structure of the active catalyst species.

This work was supported in part by NSF Grants.

(Received, July 21st, 1971; Com. 1265.)



peroxide (see Table) or Vazo.[‡] Equally surprising is the fact that if the catalyst is treated with benzoyl peroxide

[‡] E. I. du Pont de Nemours and Company, trademark for azo-bis-isobutyronitrile.

¹ D. S. Wulfman, F. C. Carman, B. G. McGiboney, E. K. Steffen, and B. W. Peace, *Preprints, Division of Petroleum Chemistry, Amer. Chem. Soc.*, 1971, 16 (1), B81.

² W. R. Moser, *J. Amer. Chem. Soc.*, 1969, 91, 1135, 1141.

³ To be published elsewhere.

⁴ D. S. Wulfman, B. W. Peace, and E. K. Steffen, *Chem. Comm.*, 1971, in the press.

Chemical Communications, 1360(1971).

Homogeneous Copper(I) Catalysed Decomposition of Dimethyl Diazomalonate. The Role of the Counter Ion in Determining the Effective Spin Multiplicity

By D. S. WULFMAN,* B. W. PEACE, and E. K. STEFFEN

(Department of Chemistry, University of Missouri-Rolla, Rolla, Missouri 65401)

Summary The reactions of olefin-dimethyl diazomalonate-trialkyl phosphite-copper(I) halide (catalyst) systems proceed *via* displacement of halide from the soluble catalyst, and this step appears to be rate determining; the leaving group ability of the anion influences the effective spin multiplicity distribution of the carbenoid species.

We report a direct correlation between the effective spin multiplicity of a carbenoid reagent and the leaving group

ability of the counter ion when the soluble catalyst systems, copper(I) salt-trialkyl phosphites,^{1,2} are used to decompose dimethyl diazomalonate. We have also found that the addition of common anions drastically depresses the yields of all identifiable products.

We have observed the uncommon phenomenon of C-H insertion at the most substituted allylic position with concomitant rearrangements when copper catalysts were employed,³ indicating that such systems proceed in part *via* triplet-like carbenoid species (Table I).† The formation

TABLE I

Effect of method of carbene generation on product distribution with 1-methylcyclohexene as substrate

			(III)		(IV)		(V)		(VI)		(VII)	
			Actual	Relative	Actual	Relative	Actual	Relative	Actual	Relative	Actual	Relative
Cu	22.9	1.00	1.23	0.054	18.5	0.810	4.13	0.180	5.64	0.122
CuCl	19.1	1.00	1.45	0.076	17.5	0.915	3.76	0.197	4.83	0.125
CuSO ₄	24.8	1.00	2.49	0.100	24.0	0.965	6.07	0.244	7.36	0.146
(MeO) ₃ P-CuCl	29.6	1.00	2.30	0.077	26.0	0.878	10.7	0.360	5.15	0.086

† The data in Tables 1—3 were obtained as follows: a solution of 0.02 mol of dimethyl diazomalonate in 0.25 mol of olefin was added at the rate of 6 drops per min to 0.25 mol of olefin under reflux containing the catalyst. After 24 h at reflux, the excess of olefin was removed by distillation and the residue analysed by g.l.c. using diglyme as an internal standard.

of allylic hydrogen insertion products together with rearrangement products clearly establishes the presence of either a radical or zwitterionic process. The variation with counter ion establishes a competition between the apparent triplet process and singlet process.

be hesitant to accept the presence of appreciable amounts of ionized material in the reaction mixture and would be looking for an alternate explanation except that the added salts were nearly completely soluble in the systems (Table 3).

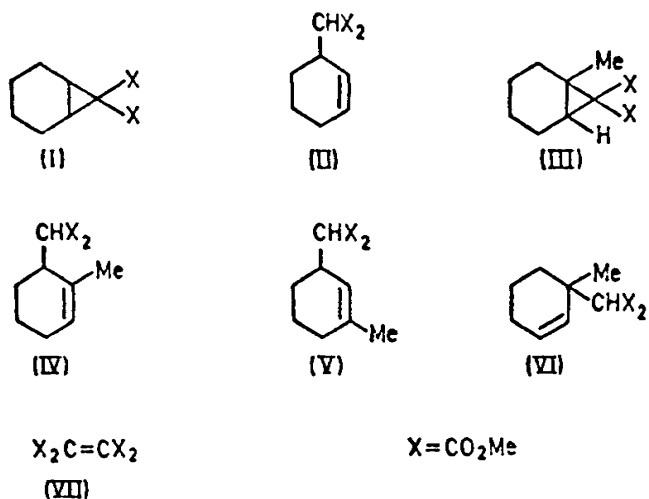
TABLE 2
Effect of counter ion upon the product distribution with cyclohexene as substrate

0.14 mmol (MeO) ₃ P-CuZ			(I)		(VII)		(II)	
			Actual	Relative	Actual	Relative	Actual	Relative
Z = BF ₄ ^a	59.3	1.00	10.1	0.084	8.05	0.136
I	73.4	1.00	17.9	0.122	7.40	0.101
Br	68.5	1.00	21.1	0.152	6.75	0.097
Cl	63.7	1.00	18.4	0.144	4.67	0.074
SCN	28.2	1.00	18.3	0.032	1.81	0.064
CN	41.3	1.00	11.2	0.013	0.93	0.023

^a Concentration less than 0.14 due to decomposition during transfer.

TABLE 3.
Effect of additives upon product distribution with cyclohexene as substrate

Catalyst	Additive	(I)		(VII)		(II)	
		Actual	Relative	Actual	Relative	Actual	Relative
(MeO) ₃ P-CuI	None	73.40	1.00	17.90	0.122	8.05	0.136
(MeO) ₃ P-CuI	Me ₄ NI	3.40	1.00	0.00	—	7.23	0.120
(MeO) ₃ P-CuI	Me ₄ NBF ₄	65.00	1.00	16.08	0.123	5.11	0.078



A direct correlation exists between the extent of allylic C-H insertion and the leaving group ability of the counter ion (Table 2) as defined in nucleophilic substitution reactions at saturated carbon. It is of interest that the addition of one equivalent of tetramethylammonium iodide to the trimethyl phosphite-copper(I) iodide system almost completely suppressed the formation of norcaradiene and insertion products whereas tetramethylammonium fluoroborate had no appreciable effect. Similar effects were observable with the chloride. These data suggest that displacement of the counter ion by diazo-compound takes place in the rate-determining step or in a pre-equilibrium step. We would

None of these results requires invoking a complex involving olefin, catalyst, and diazo-compound or carbene as suggested by Moser.² Such complexes do seem likely on the basis of precedents. The relative reactivities of increasingly substituted olefins parallels the stability of copper(I) halide-substituted acrylic acid complexes.⁴ In direct contrast with the photogenerated dimethoxycarbonyl-carbene,³ the copper catalyzed species exhibits a reduced reactivity towards increasingly substituted C-C double bonds. Thus the relative reactivities of the series, cyclohexene, 1-methylcyclohexene, and 1,2-dimethylcyclohexene are 5:1: < 0.01. The olefins are clearly participating in the solubilization of the catalyst aggregates and are at least part of an outer co-ordination sphere. The results clearly reveal that the potential carbene is intimately associated with the catalyst and that the anion has a strong influence upon the spin multiplicity of the resulting carbenoid species.

The existing data can best be explained by a scheme involving attack of the diazo-compound upon the complex, displacement of the associated anion, loss of nitrogen from the resulting diazonium ion, displacement of the electronically deficient carbene by the anion, and subsequent addition to olefinic substrate. An alternate explanation may involve the degree of metal-metal orbital overlap in the catalyst aggregates² influencing the multiplicity.

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² W. R. Moser, *J. Amer. Chem. Soc.*, 1969, **91**, 1135, 1141.

³ Musso (H. Musso and U. Beithan, *Ber.*, 1964, **97**, 2282) reported the isolation of up to 20% of the related benzenes from dihydrobenzenes as well as a comparable amount of malonic ester. Moser² reported no C-H insertion with diazoacetic ester.

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⁵ G. Karustis, Ph.D., Yale University, 1968; M. Jones, jun., A. Kolczycki, jun., and K. F. Hummel, *Tetrahedron Letters*, 1967, 183; J. A. Berson, D. R. Hartter, D. R. Klinger, and P. W. Grubb, *J. Org. Chem.*, 1968, **33**, 1669.